STUDY ON SUBCLINICAL HYPOTHYROIDISM- PREVALENCE AND ASSOCIATED FACTORS IN ELDERLY PATIENTS

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CERTIFICATE

This is to certify that the dissertation titled **"STUDY ON SUBCLINICAL HYPOTHYROIDISM-PREVALENCE AND ASSOCIATED FACTORS IN ELDERLY PATIENTS"** is the bonafide original work of **Dr.H.SABARI ANAND**, in partial fulfillment of the requirements for **M.D. Branch – XVI (Geriatric Medicine)** Examination of the **Tamilnadu DR.M.G.R. Medical University** to be held in **MARCH 2010**. The Period of study was from 2007 to 2009.

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DECLARATION

I, **Dr.H.SABARI ANAND**, solemnly declare that dissertation titled **"STUDY ON SUBCLINICAL HYPOTHYROIDISM- PREVALENCE AND ASSOCIATED FACTORS IN ELDERLY PATIENTS"** is a bonafide work done by me at Madras Medical College and Government General Hospital, Chennai, during 2007 to 2009 under the guidance and supervision of **Dr.B.KRISHNASWAMY M.D.,** Professor and Head, Department of Geriatric Medicine, Madras Medical College, Chennai.

This dissertation is submitted to the **Tamilnadu Dr. M.G.R Medical University**, towards partial fulfillment of requirements for the award of **M.D. Degree (Branch –XVI) in Geriatric Medicine.**

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CONTENTS

INTRODUCTION

Ageing is an inevitable process that converts young adults into older adults with deteriorating physiological fitness and progressively increasing risks of illness and death. The ageing of the endocrine system is characterised by the progressive loss of reserve capacity and impaired homeostatic regulation. These changes may not be clinically apparent under baseline conditions and the presenting manifestations are often nonspecific or muted or atypical or subtle.

Thyroid dysfunction is among the most common endocrine disorders in the elderly second only to Diabetes mellitus. Hypothyroidism is the most frequent thyroid dysfunction. The clinical manifestations may be less obvious in the setting of somatic complaints and other conditions related to ageing. More often it is diagnosed biochemically on evaluation for other co-morbid illnesses rather than clinically.

Subclinical hypothyroidism is the most common form of hypothyroidism in elderly. It is defined as a biochemical state characterised by serum Thyroid Stimulating Hormone (TSH) concentration above the statistically defined upper limit of the reference range when serum free Thyroxine (FT_4) concentration is within its reference range in the presence of few or no definitive clinical signs or symptoms suggestive of hypothyroidism.

The prevalence of subclinical hypothyroidism is age dependant. In geriatric populations it has been reported to range from 5.9% to 35% depending on health status, patient characteristics and patient selection procedures. Older women are

at greater risk for subclinical hypothyroidism than older men. Many studies proved that the prevalence of subclinical hypothyroidism was more than three fold increased in older women than in older men.

Subclinical hypothyroidism is most commonly an early stage of overt hypothyroidism. Progression to overt hypothyroidism ranges from 5 to 20 percent per year in patients with high titres of thyroid antibody levels and slightly elevated Thyrotropin (TSH) levels.

Patients with subclinical hypothyroidism may have increased levels of total and LDL cholesterol atleast slightly higher than euthyroid patients. The effects of dyslipidemia are less pronounced than in overt disease but predispose these patients to the development of severe cardiac disease.

Cardiovascular abnormalities associated with subclinical hypothyroidism include an increased two to three fold risk for myocardial infarction, left ventricular diastolic and endothelial dysfunction. Left ventricular ejection fraction is similar to euthyroid state at rest, but reduced with exercise.

In terms of neuropsychiatric function, the results have been mixed, with some studies suggesting increased rates of anxiety, depression, or cognitive impairment in subclinical hypothyroidism and some studies failed to show significant difference between euthyroid and subclinical hypothyroidism groups.

Given the difficulty of diagnosing thyroid failure in the elderly based on

clinical suspicion, it has been suggested that TSH tests be included in routine thyroid function screening in the geriatric population, but there is controversy about the clinical significance of detecting and treating subclinical hypothyroidism in the elderly. The efficacy of routine TSH screening in the general elderly population is questionable because of the lack of evidence from randomized control trials demonstrating that treatment of asymptomatic patients improves outcomes of subclinical hypothyroidism.

The purpose of this study was to estimate the prevalence of unrecognized subclinical hypothyroidism in elderly patients in a tertiary care setting. This study was also an attempt to acknowledge the associated factors of subclinical hypothyroidism.

AIM OF THE STUDY

1. To estimate the prevalence of subclinical hypothyroidism in elderly patients attending Geriatric Outpatient Department (Tertiary care centre).
2. To study the relationship between subclinical hypothyroidism & coronary artery disease.
3. To study the association between subclinical hypothyroidism & lipid levels.
4. To study the correlation of subclinical hypothyroidism & cognitive decline.
5. To study the association between subclinical hypothyroidism & depression.

REVIEW OF LITERATURE

THE THYROID GLAND

ANATOMY

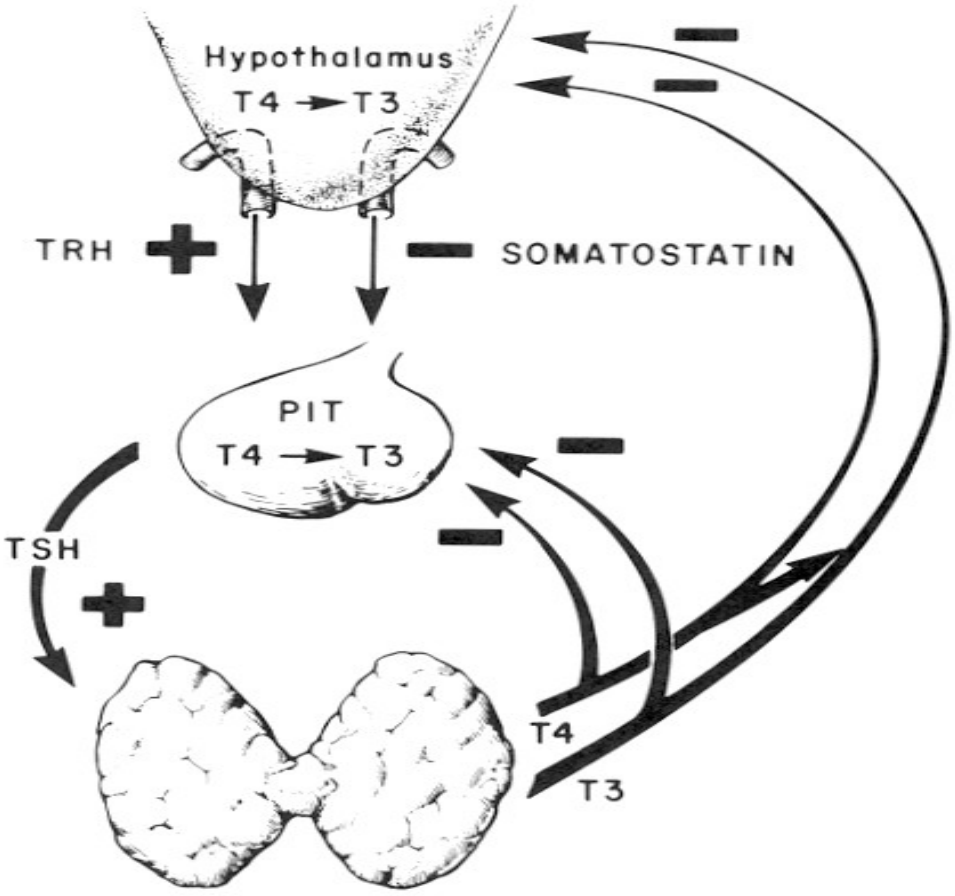
Thyroid is a small butterfly- shaped gland located anterior to the trachea between the cricoid cartilage and the suprasternal notch. The normal thyroid gland is 12-20 g in size, highly vascular and soft in consistency. Four parathyroid glands, which produce parathyroid hormone are located posterior to each pole of the thyroid.

The thyroid gland develops from the floor of the primitive pharynx during the third week of gestation. The developing gland migrates along the thyroglossal duct to reach its final location in neck. The thyroid gland consists of numerous spherical follicles composed of thyroid follicular cells that surround secreted colloid. The colloid is a proteinaceous liquid containing large amounts of thyroglobulin, the protein precursor of thyroid hormones.

PHYSIOLOGY

The hypothalamus secretes Thyrotropin Releasing Hormone (TRH) which stimulates production of Thyroid Stimulating Hormone (TSH) from the anterior pituitary. TSH in turn, stimulates synthesis and secretion of thyroxine (T4) and triiodothyronine (T3) from the thyroid. These thyroid hormones (T3&T4) feed back to inhibit TRH and TSH production.

Hypothalamic-pituitary-thyroid gland axis



This thyroid axis is a classic example of endocrine feedback loop. TRH is the major positive regulator of the axis and the “set point” of the axis is established by TSH.

Thyroid hormones (T3&T4) are derived from thyroglobulin, a large iodinated glycoprotein. After secretion into the thyroid follicle, thyroglobulin is iodinated on tyrosine residues that are subsequently coupled via an ether linkage. Reuptake of thyroglobulin into the thyroid follicular cell allows proteolysis and the release of newly synthesised T3 & T4. The entire process is triggered by the action of TSH with TSH receptor situated on the membrane of thyroid follicular cell.

Thyroid hormones transport &metabolism

T4 is secreted from the thyroid gland in about 20 fold excess over T3. Both hormones are bound to plasma proteins, including thyroxine-binding globulin (TBG), transthyretin (TTR) and albumin. When the effects of the various binding proteins are combined, approximately 99.98 % of T4 and 99.7% of T3 are protein-bound. T3 is less tightly bound than T4 and so the amount of unbound T3 is greater than unbound T4 in spite of less total T3 in the circulation.

T4 may be thought of as a precursor for the more potent T3. T4 is converted to T3 by the deiodinase enzymes (Type I, II, III) located in various tissues. Thyroid hormones (T3 & T4) bind with high affinity to nuclear thyroid hormone receptors (TRs) which are expressed in most tissues. T3 is bound with 10 to 15 times greater affinity than T4, which explains its increased hormonal potency.

It is important to note that the homeostatic mechanisms that regulate the thyroid axis are directed toward maintenance of normal concentrations of unbound hormones.

Actions of thyroid hormones

It is likely that all cells in the body are targets for thyroid hormones. Thyroid hormones have profound effects on many physiologic processes such as development, growth and metabolism.

Growth:

Thyroid hormones are clearly necessary for normal growth as evidenced by the growth-retardation observed in thyroid deficiency. The growth-promoting effect of thyroid hormones is intimately intertwined with that of growth hormone (GH).

Metabolism:

Thyroid hormones stimulate diverse metabolic activities (carbohydrate & lipid) in most of the tissues, leading to an increase in basal metabolic rate. One consequence of this activity is to increase body heat production, which result from increased oxygen consumption and rates of ATP hydrolysis. By the way of analogy, the action of thyroid hormones is akin to blowing on a smouldering fire.

Cardiovascular system:

Thyroid hormones mimic ß-adrenergic actions like increasing heart rate, cardiac contractility and cardiac output. They also promote vasodilatation, which leads to enhanced blood flow to many organs.

Central nervous system:

Both decreased and increased concentrations of thyroid hormones lead to alterations in mental state. Too little thyroid hormone make the individual feel mentally sluggish, while too much induces anxiety and nervousness.

Reproductive system:

Normal reproductive behaviour and physiology is dependent on having essentially normal levels of thyroid hormone.

The thyroid hormones also play a vital role in water and electrolyte

balance, bone demineralisation, immune regulation in the intestine and can also alter the actions of other hormones &drugs.

AGEING CHANGES OF THYROID

The structural and functional changes of the thyroid gland that occur with ageing are controversial. There is increased nodularity, fibrosis, and lymphocytic infiltration of the thyroid gland with ageing. Although the physiology of the pituitary-thyroid axis is altered in the course of normal ageing of most individuals, the ability of the axis to respond to stress is unaltered and normal thyroid function is maintained over the lifespan.

As the age advances, several changes occur in the hypothalamic-pituitary gland axis with respect to thyroid function. The secretory response of TSH to TRH stimulation in ageing persons has been reported to be decreased to 38% of the values in young persons. This may be an adaptive mechanism to the reduced need for thyroid hormone in older population.

The serum TSH concentration has been either unchanged, lowered or increased with ageing in various reports. This may be explained by the heterogeneity of the populations studied.

In a study of healthy centenarians (age range 100 – 110 years), the median serum TSH level was lower than that of older individuals (age range 65 – 80 years). The median serum TSH levels drift upwards very slowly with age, but remain in normal limits in the absence of disease. Lower TSH levels seen in institutionalised patients and in very advanced old age (>95 years) are probably due to illnesses.

TSH levels rise about 50% in the late evening before the onset of sleep. Sleep attenuates this nocturnal peak of TSH secretion and sleep deprivation exaggerates the nocturnal TSH secretion. The diurnal variation of TSH levels has been reported to be absent in elderly.

The rate of thyroxine (T4) production is decreased, but peripheral degradation of T4 is also reduced. This tends to maintain a constant serum concentration of T4 throughout life. The uptake of iodine by the thyroid gland is also reduced with ageing by more than 50% when compared with young adults.

Autoimmune damage to the thyroid increases with ageing and is associated with abnormally increased levels of circulating thyroid autoantibodies.

Human ageing and thyroid hormone economy

- ↓ peripheral degradation of thyroid hormones
- ↓ total T4 production
- ↔ serum T4 concentration
- ↓ conversion of T4 to T3
- ↔↓ serum T3 concentration
- ↔ serum TBG concentration
- ↔ thyroid gland response to TSH
- ↓ pituitary TSH secretory response to TRH
- ↓ diurnal variation of TSH
- ↓ thyroid iodide clearance
- ↔ basal metabolic rate (corrected for metabolic cell mass)

↓ decreased

↔ unchanged

THYROID DISIORDERS

The thyroid disorders are broadly classified and grouped into 4 categories. They are

1. Hyperthyroidism
2. Hypothyroidism
3. Nodular thyroid disease
4. Thyroid neoplasms

The first two are due to the abnormalities in the production of thyroid hormones. Based on these abnormalities, the classification can be modified functionally as

- Hyperthyroidism
- Subclinical hyperthyroidism
- Hypothyroidism
- Subclinical hypothyroidism

The term ‘subclinical’ denotes the laboratory finding of these hormonal abnormalities with either absent or very minimal clinical findings of the corresponding overt disease.

Hormone changes in thyroid dysfunction

Hyperthyroidism

TSH – undetectable FT3, FT4 – increased

Subclinical hyperthyroidism

TSH – undetectable FT3, FT4 – normal

Hypothyroidism

TSH – increased FT3, FT4 – decreased

Subclinical hypothyroidism

TSH – increased FT3, FT4 – normal

The hormone levels always do not satisfy the above mentioned pattern and thus complicating the diagnosis. The conditions include the secondary causes for either hyper- and hypo- thyroidism, thyroid hormone resistance, poor compliance of patients with thyroxine replacement in hypothyroidism, transient stages of auto-immune

thyroid disease and sick euthyroidism or non- thyroid illness.

Sick euthyroid syndrome

The term sick euthyroid syndrome or non- thyroid illness (NTI) refers to serum thyroid hormone concentrations secondary to the physiological stress of severe illness in the absence of underlying thyroid disease. The understanding of the effect of NTI on thyroid function tests is very important especially in the elderly who have multiple other comorbid illnesses. The changes depend on the severity of the illness and the period at which the test is undergone (during acute illness or in recovery period).

The most common hormone pattern (25% to 50%) in NTI is a decrease in total and unbound T3 levels and normal levels of T4 and TSH. In more severe illness, T4 level also falls and the decreases in the thyroid hormone levels may be an adaptation to spare the patient from the catabolic effect of thyroid hormones during the periods of extreme stress. The severity of the illness correlates with the degree of fall in the serum T3 concentration. The low serum T4 state correlates with poor prognosis.

Fluctuation in the TSH level also creates a challenge in the interpretation of thyroid function tests in sick patients. Serum TSH level usually remains normal except in the patients receiving dopamine or glucocorticoids, which reduce serum TSH levels. During the recovery period TSH level remains normal. There is increased reverse

T3 (rT3) level either due to increased production or impaired clearance as a consequence of the decreased 5`-deiodinase with illness.

Any severe illness can induce changes in thyroid hormone levels and this makes the diagnosis of NTI challenging. The features to consider include previous history of thyroid disease and thyroid function tests, course of patient's illness, documentation of medications that affect thyroid function or hormone levels and the measurement of rT3 together with unbound thyroid hormones and TSH. The diagnosis of NTI is frequently presumptive and only the resolution of the test results with clinical recovery can clearly establish the disorder.

SUBCLINICAL HYPOTHYROIDISM

The term subclinical hypothyroidism was coined by Bastenie et al in 1967. Evered and colleagues subsequently described a similar group of asymptomatic individuals in whom conventional tests of thyroid function showed nothing abnormal but they were all found to have a raised serum thyrotropin concentration.

Since then, hundreds of articles have been published on this topic, but physicians are no closer to understanding whether this mild, usually asymptomatic form of hypothyroidism presents a clinical risk, requiring screening for detection and thyroid hormone treatment, or whether screening and therapy are unnecessary and possibly even counterproductive (Cooper DS; JAMA 2004).

Definition

Subclinical hypothyroidism is defined as a biochemical state characterised by serum Thyroid Stimulating Hormone (TSH) concentration above the statistically defined upper limit of the reference range when serum free T_4 (FT_4) concentration is within its reference range in the presence of few or no definitive clinical signs or symptoms suggestive of hypothyroidism.

Other causes of an elevated serum TSH must be excluded like recovery phase of sick euthyroid syndrome; recent adjustments in levothyroxine dosage with failure to reach a steady state, particularly in poorly compliant patients; or during

recovery from destructive thyroiditis, including post-viral subacute thyroiditis; untreated primary adrenal insufficiency; patients receiving recombinant human TSH injections; thyroid hormone resistance syndrome and the presence of TSH antibodies leading to falsely elevated TSH levels.

Synonyms

This term subclinical hypothyroidism has been given a variety of other names. They include:

- Mild thyroid failure
- Compensated thyroid failure
- Early hypothyroidism
- Latent hypothyroidism
- Mild hypothyroidism
- Asymptomatic hypothyroidism
- Pre-clinical hypothyroidism
- Hidden hypothyroidism

Clinical features can be absent to very few suggestive of hypothyroidism and hence the term subclinical is being replaced in many parts of the world. Although the term subclinical hypothyroidism is widely used, mild hypothyroidism may be more appropriate.

Prevalence

The prevalence of subclinical hypothyroidism in elderly has been reported to range from 5.9% to 35% depending on health status, patient characteristics and patient selection procedures.

The prevalence is age and gender dependant. It increases as the age advances and in females than males. The classic Whickham survey in Great Britain reported increasing prevalence of elevated TSH levels with age, upto 18% in women older than 74 years of age. In Colorado Health Fair study the prevalence of subclinical hypothyroidism is 19% in those aged older than 74 years.

In a survey in United States, the prevalence of serum TSH elevation was 8.5% in women and 4.4% in men older than age 55 years. In a study conducted by Bemben et al in Oklahoma, 14.6% of the women and 15.4% of the men had subclinical hypothyroidism in older people greater than 60 years. In a study conducted in King Abdulaziz University, Saudi Arabia, about 35% of the elderly women attended the outpatient clinic had subclinical hypothyroidism.

Etiology

Subclinical hypothyroidism is caused by the same disorders of the thyroid gland as those that cause overt hypothyroidism. The following table enumerates the

causes of subclinical hypothyroidism.

Chief among these is chronic autoimmune thyroiditis (Hashimoto's disease), which is commonly associated with increased titers of antithyroid antibodies, such as antithyroid microsomal antibodies (antithyroid peroxidase) and antithyroglobulin antibodies. This disorder is suspected when thyroid enlargement is observed, but antithyroid antibodies may also be associated with atrophy of the thyroid and hypothyroidism. Another common cause of hypothyroidism is the treatment of Graves' disease. Thyroid failure is most common after radioactive iodine treatment, but hypothyroidism may eventually occur in 5 to 25 percent of patients treated with surgery or antithyroid drugs.

A survey of endocrinology clinic patients revealed that 57% of patients aged 55 and older presenting with primary hypothyroidism carried a diagnosis of autoimmune thyroiditis, while 32% carried a diagnosis of postsurgical hypothyroidism and 12% had a diagnosis of post-radioiodine hypothyroidism. Only 2% of the patients in this referral population presented with documented evidence of secondary hypothyroidism.

Less common causes of hypothyroidism include use of medications such as lithium and amiodarone. Pituitary failure is a cause

of secondary hypothyroidism but since, in this circumstance, the TSH level is low rather than high (and thus the direct cause of the thyroid failure), this condition cannot be diagnosed with certainty until thyroid hormone levels fall below normal, and subclinical hypothyroidism as usually defined would not be detected.

Pathophysiology

Serum TSH has a log-linear relationship with circulating thyroid hormone levels (a 2-fold change in free thyroxine will produce a 100-fold change in TSH). Thus, serum TSH measurement is the necessary test for diagnosis of mild thyroid failure when the peripheral thyroid hormone levels are within normal laboratory range. The individual range for peripheral thyroid hormones is narrower than the population reference laboratory range; therefore, a slight reduction within the normal range will result in elevation of serum TSH above the normal range.

One of the myths that surrounds subclinical hypothyroidism is that the laboratory profile of an elevated serum TSH and normal free thyroid hormone levels really represents "compensated hypothyroidism." The reasoning behind this idea is that, since the circulating levels of thyroid hormones are within the normal range with only the serum TSH being elevated, the affected subject is really euthyroid because the increased TSH is stimulating and driving the thyroid gland to produce normal thyroid hormone levels.

Certainly, elevated serum TSH levels do stimulate even a diseased thyroid

gland to produce and release more thyroid hormone. The clearance kinetics of thyroid hormones and TSH from the circulation actually makes such a conclusion inescapable. Because the half-life of T_4 is 7 days and that of T_3 is 1 day, the serum TSH, which has a half-life of less than 1 hour, would certainly be expected to return to normal if thyroid hormone levels were, indeed, normal for that individual. An elevated TSH in an individual patient, thus, means that the circulating thyroid hormone concentrations are insufficient for maintaining routine functions.

Stages of thyroid gland failure

The phenomenon of thyroid gland failure is now recognised and can be divided into four stages.

Stage a: The earliest form is identifiable only by a positive TRH test and is represented by the state of a normal FT4 level accompanied by a TSH level slightly above a given individual's set point, but within the population reference range.

Stage b: Further along the continuum of thyroid failure is that involve mild elevation of TSH (5–10 mIU/L) with normal FT4 level.

Stage c: This stage has prominent elevation of TSH above 10 mIU/L with normal FT4 level.

Stage d: The final stage of this continuum is overt thyroid gland failure or overt hypothyroidism, which is defined by a low FT_4 and an elevated TSH, usually much higher than 10 mIU/L.

The stages a, b and c are usually subclinical, stage d is overt. Stage b and c looks similar but the subjects in these two groups exhibit dissimilar characteristics. Stage c can be treated like overt even when the manifestations are subclinical.

The state of subclinical hypothyroidism may also be found in at least five distinct situations:

1. mild unrecognized thyroid failure
2. under treated overt hypothyroidism
3. over treated overt hyperthyroidism
4. transient disturbances of the thyroid axis
5. Euthyroid outliers (this term will be applied to the 2.5% of individuals possessing TSH values above the 97.5 percentile of the euthyroid distribution).

A treatment plan for subclinical hypothyroidism should rely on awareness of the underlying pathogenesis, because the five different clinical states clearly require separate therapeutic strategies.

Course of subclinical hypothyroidism

The course of the patients who are found to have an elevated TSH level without other findings can be either of the three of the following:

1. The TSH level will be normal if measured again several months later; we would then attribute the initial elevation to laboratory error or to an episode of silent thyroiditis with a transient hypothyroid phase.
2. Subclinical hypothyroidism remains unchanged.
3. Progression to overt hypothyroidism occurs at a rate of about 5 percent per year in patients with raised TSH levels and detectable antithyroid antibodies.

In selected cases (e.g., elderly patients with high titers of antithyroid antibodies), the risk of progression to overt disease may be closer to 20 percent per year. Consideration of these possible outcomes affects the decision about whether to treat or to observe without treatment.

Subclinical hypothyroidism represents an early stage of thyroid disease that will commonly progress to overt hypothyroidism. One study evaluated the natural history of mild thyroid failure in 154 female patients over a 10-yr period; 57% of patients continued to have mild thyroid failure, 34% of patients progressed to overt

hypothyroidism, and 9% of patients reverted to a normal TSH level. How many of the 9% had a transient form of thyroiditis is unclear.

In a study in men and women older than 55 years with a mean follow-up of 32 months, the TSH level normalized in 52% of those with a serum TSH of less than 10 mIU/L. A similar study that stratified subjects on the basis of anti-thyroid antibody levels reported that 80% of elderly adults with mild hypothyroidism with initial measured anti-microsomal antibody titers greater than 1:1,600 eventually progressed to develop overt hypothyroidism requiring treatment with thyroxine replacement therapy.

In the 20 year follow-up study of patients with subclinical hypothyroidism in the Whickham survey, the annual rate of thyroid failure was 4.3% in those with positive thyroid antibodies, as compared to 0.3% in thyroid antibody negative patients.

The strongest predictors of progression are the presence of high titers of antithyroid antibodies, serum TSH values greater than 10 mIU/L, a history of radioiodine ablation for Graves' disease, a history of external radiation therapy for nonthyroid malignancies, chronic lithium or amiodarone treatment.

Clinical manifestations

Signs and Symptoms of Hypothyroidism

- Weakness
- Lethargy
- Fatigue
- Dry skin
- Coarse hair
- Cold intolerance
- Constipation
- Weight gain
- Muscle cramps
- Edema of face and eyelids
- Nonpitting edema of legs
- Hoarseness
- Hearing loss
- Menorrhagia
- Slowing of return phase of reflexes (e.g., ankle jerk)
- Bradycardia

The above mentioned clinical signs and symptoms of hypothyroidism manifest when the disease is fully developed. But even in the earliest (subclinical stage), one or more of these findings may occur.

The Colorado Thyroid Disease Prevalence Study measured serum TSH levels and conducted symptom surveys in over 25,000 state residents. Elevated serum TSH values were found in 8.9% of those who were not already on thyroid hormone therapy. In response to a validated survey regarding symptoms of thyroid hormone deficiency, the 2,336 subjects who were identified as having subclinical hypothyroidism significantly.

The more often reported symptoms are dry skin (28%; $P < 0.001$), poor memory (24%; $P < 0.001$), slow thinking (22%; $P < 0.001$), muscle weakness (22%; $P < 0.001$), fatigue (18%; $P < 0.01$), muscle cramps (17%; $P < 0.001$), cold intolerance (15%; $P < 0.001$), puffy eyes (12%; $P < 0.05$), constipation (8%; $P < 0.05$), and hoarseness (7%; $P < 0.05$) than did euthyroid subjects.

It is important to note that, when euthyroid subjects experienced a mean of 12.1% of all listed symptoms, overtly hypothyroid subjects had 16.6% of these symptoms ($P < 0.05$ *vs.* euthyroid group), and subjects with subclinical hypothyroidism

reported an intermediate 13.7% of the symptoms ($P < 0.05$ *vs.* euthyroid group) (Fig. 2). This suggests a "dosage effect" between levels of thyroid hormones and symptoms.

Consistent with these findings, a Swiss study involving 332 women with hypothyroidism reported that 24% of the 93 subjects with subclinical hypothyroidism exhibited typical symptoms of hypothyroidism. These studies suggest that some patients with subclinical hypothyroidism do indeed have clinical manifestations of mild thyroid failure.

These studies also emphasize the difficulty in making the diagnosis of primary hypothyroidism using clinical symptoms alone; euthyroid subjects and patients with mild or overt hypothyroidism all had similar constellations of symptoms. Despite statistical significance in large groups, it can be difficult in an individual patient to distinguish a euthyroid subject from one with either mild or overt thyroid disease.

Adverse outcomes of subclinical hypothyroidism

The possible physiologic effects of subclinical hypothyroidism include dyslipidemia, cardiovascular risk, neurocognitive effects, and other non-specific symptoms of overt hypothyroidism.

Dyslipidemia:

Dyslipidemia is commonly found in hypothyroidism and also in subclinical hypothyroidism. Treatment of the thyroid disorder potentially improves dyslipidemia and reduces risk for cardiovascular diseases. In the absence of significant symptoms associated with subclinical hypothyroidism, dyslipidemia may be a key indicator of thyroid failure.

Although the view that overt hypothyroidism causes secondary hyperlipidemia and promotes atherosclerosis has been generally accepted, studies examining the relationships between hyperlipidemia, atherosclerosis, and subclinical hypothyroidism have yielded less convincing results. Some cross-sectional observational surveys note a higher prevalence of subclinical hypothyroidism in hyperlipidemic patients, whereas others show that subclinical hypothyroidism subjects manifest moderately (mostly up to 10%) higher average total cholesterol than controls.

In patients with full-blown hypothyroidism, serum levels of triglycerides, total cholesterol and low-density lipoprotein (LDL) cholesterol are elevated. In patients with subclinical hypothyroidism, not surprisingly, the same changes are present but are less marked and less consistent. This pattern of lipid abnormalities, of course, is important because it is a risk factor for atherosclerotic cardiovascular disease. Some

studies have shown a decrease in LDL cholesterol and total cholesterol levels after treatment with levothyroxine.

Subclinical hypothyroidism does result in small increase in low density lipoprotein cholesterol and a decrease in high density lipoprotein, changes that enhance the risk for development of atherosclerosis and coronary artery disease. The influence of subclinical hypothyroidism on lipids was directly proportional to the degree of TSH elevation. It has been estimated that an increase in the serum TSH level of 1 mIU/L is associated with a rise in the serum total cholesterol (TC) concentration of 0.09 mmol/L (3.5 mg/dl) in women and 0.16 mmol/L (6.2 mg/dl) in men.

The Whickham study observed that lipid levels were not associated with TSH elevations after age adjustment. The follow-up Whickham survey found no association between elevated serum TSH and increased risk of ischemic heart disease or dyslipidemia.

A large cross-sectional survey of 3410 elderly subjects in Maryland noted significantly elevated LDL cholesterol in subjects with subclinical hypothyroidism, but only for those with TSH higher than 10 mIU/L; no increased frequency of diagnosed atherosclerotic diseases was found in this entire cohort of SH subjects. A report from Rotterdam noted that subclinical hypothyroidism subjects actually had lower TC than

controls, but manifested increased atherosclerotic vascular disease, suggesting that factors other than TC contribute to the increased risk of atherosclerosis, although LDL was not explicitly determined. In a study conducted by Haralampos et al in Greece, patients with subclinical hypothyroidism exhibited increased Lipoprotein a (Lp a) levels compared to euthyroid patients.

Thus on considering the conflicting data of the large-scale epidemiological surveys of Whickham, Maryland and Rotterdam with respect to thyroid dysfunction and lipid levels is still debatable.

Cardiovascular diseases:

The association between overt hypothyroidism and coronary heart disease has been repeatedly observed (Becker 1985). Less evident is the role of asymptomatic mild elevation of TSH (subclinical hypothyroidism), even though it represents the majority of patients with thyroid dysfunction. There is no clear confirmational data to date that subclinical hypothyroidism causes clinical heart disease. However, mild failure of the thyroid gland, as evidenced solely by elevation of serum TSH level, may be associated with increased morbidity, particularly for cardiovascular disease and subtly decreased myocardial contractility.

In subclinical hypothyroidism both cardiac structures and function remain normal at rest, but impaired ventricular function as well as cardiovascular and respiratory adaptation to effort may become unmasked during exercise. These changes are reversible when euthyroidism is restored. Subclinical hypothyroidism does result in small increase in low density lipoprotein (LDL) cholesterol and a decrease in high density lipoprotein (HDL) cholesterol, changes that enhance the risk for development of atherosclerosis and coronary artery disease.

Flow-mediated vasodilatation, a marker of endothelial function, is significantly impaired in subclinical hypothyroidism, and decreased heart rate variability, a marker of autonomic activity, suggests hypofunctional abnormalities in the parasympathetic nervous system. In subjects with subclinical hypothyroidism after coronary revascularization, a trend toward higher rates of chest pain, dissection, and re-occlusion has been noted.

Studies have shown that patients with subclinical hypothyroidism have slowed left ventricular relaxation time, increased vascular tone at rest, and left ventricular systolic dysfunction with exercise and impaired endothelial function. In one comprehensive study of exercise capacity, patients with subclinical hypothyroidism were shown to have significant impairment of exercise-related stroke volume, cardiac index, and maximal aortic flow velocity.

A 20 year follow-up study of the original Whickham Survey found no association between initial hypothyroidism, raised serum TSH levels, or antithyroid antibodies and the development of coronary artery disease. In contrast, a more recent report from the Rotterdam Study concluded that patients with subclinical hypothyroidism have a significantly increased prevalence of aortic atherosclerosis and myocardial infarctions.

A study done by Hak et al (2000) shown that subclinical hypothyroidism independently doubled relative risk of myocardial infarction in females. Several more recent meta-analyses of observational studies found an association between subclinical hypothyroidism and coronary artery disease.

In the two new studies, thousands of patients in the U.S. and Australia agreed to be followed for a period of years, in an effort to evaluate the ability of various risk factors to predict subsequent disease. One of the lab tests measured at the beginning of these studies was the TSH level. Investigators in the U.S. study, the Health, Aging and Body Composition Study, found that patients with elevated TSH levels (at least 4.5 mIU/L) had a significantly higher risk of developing heart failure over the next 4 years than patients with normal TSH levels. In the Australian study, the Brusselton Health Study, patients with elevated TSH levels had an increased risk of hospitalization or death from coronary artery disease. In both studies, the higher the TSH level, the higher the risk. The highest risk was seen in patients with TSH levels of 10.0 mIU/L or greater. Thus, after the adjustment for multiple known coronary artery disease risk factors,

subclinical hypothyroidism can be considered as an independent and important risk factor for myocardial infarction.

Psychiatric and cognitive dysfunction:

Cognitive dysfunction can result from increased or decreased concentrations of thyroid hormones. Clinical and subclinical hypothyroidism in elderly adults are associated with decreased cognitive functioning, especially memory, visuospatial organization, attention, and reaction time. Mild variations of thyroid function, even within normal limits, can have significant consequences for cognitive function in them.

Different cognitive deficits possibly related to thyroid failure do not necessarily follow a consistent pattern, and L-thyroxine treatment may not always completely restore normal functioning in patients with hypothyroidism. There is little or no consensus in the literature regarding how thyroid function is associated with cognitive performance in the elderly. Subclinical hypothyroidism may be a predisposing factor for cognitive impairment.

Cook et al reported that elderly patients with subclinical hypothyroidism performed more poorly than euthyroid individuals on measures of verbal recall as well as on the Mini-Mental State Examination but working memory and processing speed were unaffected. In contrast, three studies failed to find cognitive impairment associated with subclinical hypothyroidism.

The possibility of reversing some aspects of the cognitive impairment associated with subclinical hypothyroidism has been demonstrated after treatment with L-thyroxine. The comprehensive study of Del Ser Quijano et al revealed that L-thyroxine treatment was associated with significant improvements on multiple cognitive measures including attention, memory, verbal fluency, and executive functions compared to control participants.

The elderly may be more vulnerable to the cognitive effects of subclinical hypothyroidism than young adults, suggesting that diagnosis and treatment may protect the aging brain from cognitive deterioration. However, it is not yet certain that favourable results obtained with young adults are predictive of favourable responses in elderly. Furthermore, different cognitive functions probably have varying sensitivity to hormonal or metabolic changes and not all the cognitive defects related to thyroid failure are completely reversible with L-thyroxine therapy.

DATA RELATED TO AGGRAVATION OF DEPRESSION, BIPOLAR DISORDER AND EFFECTS ON COGNITIVE FUNCTION HAVE BEEN PRESENTED IN SUBJECTS WITH SUBCLINICAL HYPOTHYROIDISM. THE PAQUID SURVEY AND CORRELATES OF **SUBCLINICAL HYPOTHYROIDISM IN ELDERLY** COMMUNITY RESIDENTS **IN** THE SOUTH WEST OF FRANCE FOUND THAT **IN**CREASED TSH LEVELS WERE SIGNIFICANTLY L**IN**KED WITH FEMALE SEX AND WITH THE PRESENCE OF SYMPTOMS OF DEPRESSION BUT NOT WITH IMPAIRMENT OF COGNITIVE FUNCTION.

IN A STUDY OF HEALTH STATUS, MOOD AND COGNITION IN EXPERIMENTALLY INDUCED SUBCLINICAL HYPOTHYROIDISM BY **M. H. SAMUELS ET AL,** WHEN SUBCLINICAL HYPOTHYROIDISM WAS INDUCED IN LEVOTHYROXINE TREATED HYPOTHYROID SUBJECTS, MILD DECREMENTS IN HEALTH STATUS AND MOOD WAS ESTABLISHED. MORE IMPORTANTLY, THERE WERE INDEPENDENT DECREMENTS IN WORKING MEMORY, WHICH SUGGESTS THAT SUBCLINICAL HYPOTHYROIDISM SPECIFICALLY IMPACTS BRAIN AREAS RESPONSIBLE FOR WORKING MEMORY.

Neuromuscular function:

A variety of neuromuscular complaints have all been reported to occur more frequently in patients with subclinical hypothyroidism. Objective peripheral nerve dysfunction, manifested by decreased conduction amplitude in peripheral nerves and an

abnormal stapedial reflex has been demonstrated in these patients. Skeletal muscle abnormalities, including elevated serum creatine phosphokinase levels, increased circulating lactate levels during exercise and repetitive discharges on surface electromyography have also been reported.

Pulmonary function:

Pulmonary function in the patients with subclinical hypothyroidism revealed decreased vital capacity, reduced anaerobic threshold, and decreased oxygen uptake at the anaerobic threshold.

Iodine and subclinical hypothyroidism

Dietary iodine content appears to have an impact on the prevalence of hypothyroidism in the elderly. A survey of Chinese adults living in a region of low iodine intake revealed that only 1.0% of elderly subjects studied met criteria for hypothyroidism, while a study of Eastern European nursing home residents revealed that subjects living in regions of abundant iodine intake had six-fold higher rates of hypothyroidism than subjects living in regions of low iodine intake. These findings suggest that iodine deficiency may have a protective effect against the development of hypothyroidism in the elderly.

In a study conducted in Andhra Pradesh, India, by Department of

Biochemistry, Kamineni Institute of Medical Sciences, they have noticed high prevalence of subclinical hypothyroidism in subjects consuming excessive amounts of iodine. In the present scenario of the post –iodination status in India, excessive iodine intake should also be considered as an etiology of hypothyroidism.

Screening

Despite recognition of this condition and the observation that a small percentage of these patients advance to overt hypothyroidism each year, controversy continues over whether elderly individuals should be screened for subclinical hypothyroidism. The decision about whether to screen patients for this disorder is clouded by inconsistent evidence of any benefit from early treatment.

American Thyroid Association has endorsed screening for this disorder, but others, such as the US Preventive Services Task Force, have advised against routine screening. In addition, although the American College of Physicians recognises that screening women older than 50 years for hypothyroidism may have some value, they specifically note that the benefit of treating patients with subclinical hypothyroidism has not been evaluated. The decision about whether to screen patients for subclinical hypothyroidism is clouded by inconsistent evidence of any benefit from early treatment.

Recommendations of eight organisations regarding screening of asymptomatic adults for thyroid dysfunction

ORGANISATION	SCREENING RECOMMENDATION
1.American Thyroid Association	Women and men > 35 yr of age should be screened every 5 yr
2.American Association of Clinical Endocrinologists	Older patients, especially women should be screened
3.College of American Pathologists	Women >50 yr of age should be screened if they seek medical care ; all geriatric patients should be screened on admission & at least every 5 years
4. American academy of Family physicians	Patients >60 yr of age should be screened
5. American college of Obstetrics & Gynaecology	Women in 'high risk groups' should be screened starting at 19 yr of age
6. American college of Physicians	Women >50 yr of age with an incidental finding suggestive of symptomatic thyroid

The upper limit of serum TSH level

Lowering the upper limit of normal for the serum TSH level from 5.0 to 3.0 or even 2.5 mIU/L has been proposed, but such proposals have been met with substantial critique. The strongest argument in favour of lowering the upper limit of normal for the serum TSH level is the higher level of antithyroid antibodies detected in persons with a serum TSH level between 3.0 and 5.0 mIU/L and the higher rate of progression to clinical thyroid disease.

After exclusion of persons with goitre, antithyroid antibodies, and a family history of thyroid disease, the mean serum TSH is 1.5 mIU/L. The serum TSH distribution curve is not Gaussian; there is a tail end at the upper limits of normal. If the distribution curve is extrapolated to be Gaussian, then the upper limit for the 97.5th percentile will be 2.5 mIU/L.

The argument against lowering the upper limit of normal for TSH values is that more patients would be diagnosed with hypothyroidism without any clinical or therapeutic benefit from this diagnosis. Decreasing the upper limit of the TSH reference range to 3.0 mIU/L results in more than a 4-fold increase in diagnosis of hypothyroidism among patients without history of thyroid disease seen in a tertiary medical centre. No clear evidence supports a benefit for intervening at these levels of TSH.

Recent re-analysis of the data from the National Health and Nutrition Examination Survey III study has suggested that serum TSH distribution progressively shifts toward higher concentrations with age and that the prevalence of subclinical

hypothyroidism may be significantly overestimated in older age groups unless an age-specific range for TSH is used. In a recent study of 766 persons with negative findings on antithyroid antibody assay, normal findings on thyroid ultrasonography, and no evidence of thyroid disease, Hamilton et al determined a serum TSH level of 4.1 mIU/L to be the upper reference limit. This value is more compatible with clinical experience and is a reasonable compromise.

The lack of evidence for a benefit from levothyroxine therapy at the level of 3.0 to 4.0 mIU/L makes keeping the upper limit of TSH at 4.0 to 5.0 (depending on the laboratory) more reasonable.

Treatment

There is considerable evidence suggesting that the subjects with subclinical hypothyroidism who would benefit most from L-thyroxine therapy are those with TSH levels exceeding 10 mIU/L. Such individuals constitute the minority of those with subclinical hypothyroidism in all large-scale epidemiological studies that have stratified TSH levels.

The majority of subjects with subclinical hypothyroidism, however, have slight elevations of TSH ranging between 5 and 10 mIU/L, and they have minimal, often non-significant, metabolic abnormalities. They are either affected by mild incipient

thyroid failure for which L-thyroxine therapy has not been shown to convey recognizable benefits, or they may simply represent "euthyroid outliers" in the 2.5% tail above the upper limit of the normal TSH reference range, in which case L-thyroxine treatment would be inappropriate.

Despite this, some groups have recommended that all elderly patients with subclinical hypothyroidism and a TSH level greater than 10 mIU/L receive hormone replacement therapy (HRT) and that HRT can be considered for older people with compatible symptoms and a TSH level between 5 and 10 mIU/L. To date, no randomized controlled trials have provided evidence to support these recommendations, and there is reason to suspect that they may be flawed.

From the animal models of ageing, it is known that restriction in energy intake, with its associated reduction in metabolic rate, results in increased longevity. Administration of thyroid hormone could theoretically accelerate the ageing process by increasing metabolic rate. In addition, age-related hormone deficiencies (e.g., growth hormone) are not necessarily associated with poor outcomes. In fact, restoring hormone levels in older patients to those of younger patients may have adverse consequences.

For patients with sustained increases above 10 mIU/L, there is uniform agreement that thyroxine therapy is indicated. Therapy for milder forms of

hypothyroidism is controversial. Some randomized clinical trials favour therapy for mild thyroid failure, but they are inconclusive because they lack stratification for the subgroup of patients with TSH levels below 10 mIU/L. For this subgroup, individualized management is recommended.

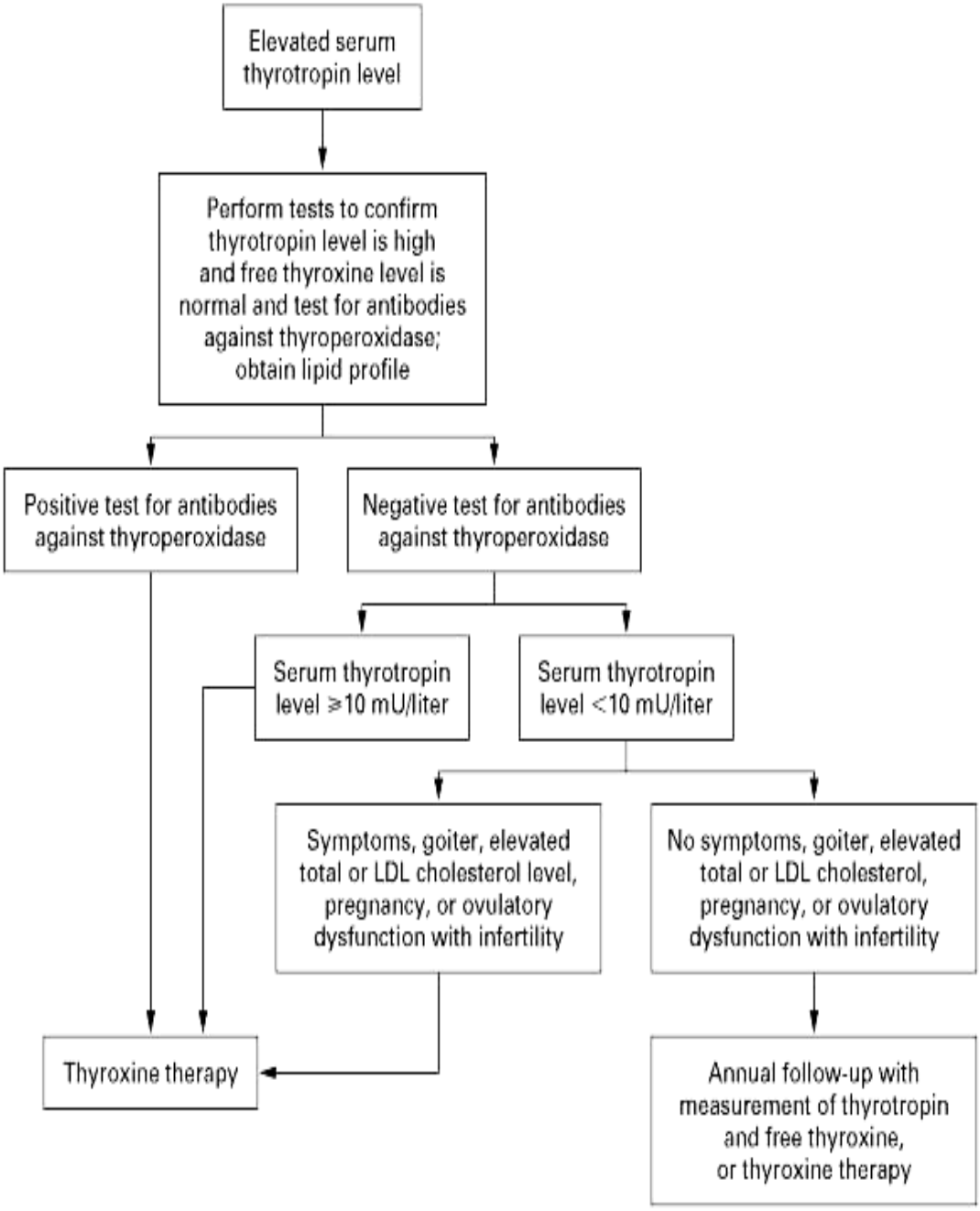
Recent studies have reported that "high normal" TSH values may be associated with modest increases in serum cholesterol levels and that serum cholesterol levels improve when TSH values are reduced from the high end to the low end of the normal range with L-thyroxine supplementation. In patients with subclinical hypothyroidism and CAD, L-thyroxine therapy can be beneficial in diminishing lipid abnormalities in those with lower body mass index, briefer duration of CAD, and higher levels of cholesterol at baseline. L-thyroxine treatment appears to have a preventive effect on the disturbance of lipid metabolism in patients with subclinical hypothyroidism, especially in patients with serum TSH levels above 10 mIU/L (Miura S, et al).

A recent consensus statement issued by an expert panel recommended that cases of mild hypothyroidism presenting with TSH levels ranging from 4.5-10.0 mIU/L be treated on a provisional basis, with continuation of therapy predicated on clear evidence of improvement in symptoms consistent with thyroid hormone deficiency.

Factors favouring L-thyroxine therapy in elderly patients with TSH level of 5 to 10 mIU/L are:

1) Patient preference
2) Two TSH levels >8 mIU/L
3) Goitre
4) Bipolar disorder, depression
5) Presence of antithyroid antibodies
6) Convincing family history of thyroid disease
7) Severe hyperlipidemia not previously diagnosed
8) Therapeutic trial for possible hypothyroid symptoms
9) Strong habit of tobacco use
10) Progressive TSH increase

An Algorithm for the Management of Subclinical Hypothyroidism



Levothyroxine therapy

Patients with subclinical hypothyroidism, because of the minimal extent

of the thyroid hormone deficiency, may be controlled with total daily dosages of levothyroxine as low as 25 to 50 µg. This initial dosage should be maintained for six to eight weeks before a TSH measurement is repeated to guide adjustment of the levothyroxine dosage.

The goal is to maintain the TSH level within normal limits; the dosage of levothyroxine should be increased if the TSH level remains above normal and should be decreased if the TSH level falls below normal. Serum TSH should be checked after 8 weeks and the dose should be adjusted. Once a normal serum TSH level has been achieved, TSH should be measured again after 6 months and then annually. The benefits of fine-tuning levothyroxine therapy to achieve lower levels of serum TSH should be weighed against the possibility of adverse effects of overzealous levothyroxine therapy.

MATERIALS AND METHODOLOGY

Setting

Outpatient settings of Department of Geriatric Medicine, Government General Hospital, Chennai-3 (Tertiary care centre).

Study Design

Cross-sectional study

Period of study

February 2009 to October 2009 (9 months)

Inclusion Criteria

All patients attending Geriatric outpatient clinic during the above mentioned period (maximum of 90 patients).

Exclusion criteria

1. Patients with recent surgery, recent myocardial infarction and with recent acute illness followed by hospitalisation in the past 6 months.

2. Patient who were already diagnosed to have any thyroid dysfunction (hypo- and hyper- thyroidism) or received radiotherapy over head and neck for any cause.

Sample size

A total of 90 patients were studied.

Details of the study

All the 90 patients were randomly selected from the outpatient clinic of Department of Geriatric Medicine, Government General Hospital, Chennai-3(Tertiary care centre). The patients divided into 3 age groups (60-69 years, 70-79 years, and 80+ years). 15 males &15 females were included in each age group.

All the study subjects were interviewed and the medical history was obtained. The patients were explained of the methods and objectives of the study and an informed consent was obtained from them. A brief general examination including height and weight measurement was carried out as per the particulars mentioned in the proforma.

Blood Pressure (BP): Blood pressure was measured twice in the sitting position on the right arm, using standard mercury sphygmomanometer to the nearest 2 mm of mercury.

Coronary Artery Disease (CAD): CAD was documented if the person had prior coronary revascularization, coronary angiographic evidence of significant CAD, a documented history of myocardial infarction, electrocardiographic evidence of Q-wave myocardial infarction, or on treatment for CAD documented by cardiology department. All electrocardiograms were reviewed for evidence of myocardial infarction.

Co-morbid illnesses: Patients with only documented evidence of the co-morbidities like Diabetes Mellitus (DM), Systemic Hypertension (SHT), Peripheral Vascular Disease (PVD) and Cerebrovascular Accident (CVA) were taken into consideration.

Geriatric Depression Scale: The original Geriatric Depression Scale was a 30- item questionnaire which was time consuming and challenging for both patient and the examiner. Later versions retain only the most discriminating questions and their validity approaches that of the original form. The most common version in general geriatric practice currently is the 15 –item questionnaire.

The test was undertaken orally. Patients were asked to reply indicating how they have felt over the past week. A clear yes or no reply was obtained. Each depressive answer (bold) was given a score of 1.

Scoring intervals

0-4 No depression

5-10 Mild depression

11+ Severe depression

Clock drawing Test & Mini-Cog: Clock drawing test (CDT) is widely accepted and well validated screening tool for dementia. Their strength is in the brisk assessment of multiple cognitive domains including long-term memory, auditory and visual processing, motor planning, execution, etc. The patient was asked to draw a clock face showing a named time and then assessed. This has great value in ruling in or ruling out significant cognitive dysfunction.

The Mini- Cog test combines a 3- item recall test with a CDT. This is a sensitive and specific test, and largely uninfluenced by level of education, language or other cultural factors.

Administration

- The patient was asked to attend carefully and to remember three unrelated words (of the examiner's choice) and then repeat the words to confirm registration.
- The patient was asked to draw a clock face on a blank sheet of paper showing a specific time. Instructions may be repeated, but no more detail given.
- The patient was asked to repeat the three words.

Scoring

- One point was given for each word correctly recalled after CDT.
- The CDT is normal if all numbers (1-12) were present in correct sequence and position.

Positive screen for dementia - score of 0 & 1 or 2 with an abnormal CDT.

Negative screen for dementia - score of 3 & 1 or 2 with normal CDT.

The patients were asked to come to the outpatient clinic on the next day morning with overnight fasting and around 5 ml of venous blood samples drawn were used for biochemical laboratory analysis. The laboratory examinations included estimation of Total cholesterol, High Density Lipoprotein (HDL), Triglycerides (TG) and Thyroid stimulating hormone (TSH) &free thyroxine (FT4).

Dyslipidemia: Dyslipidemia was diagnosed if the serum total cholesterol was ≥200 mg/dl, if the serum high-density lipoprotein (HDL) cholesterol was <40 mg/dl, or if the serum triglycerides was ≥200 mg/dl.

Subclinical hypothyroidism: Subclinical hypothyroidism was diagnosed if the serum TSH level was elevated and the serum T_4 level was in the normal range.

Comparison between patients with subclinical hypothyroidism and without subclinical hypothyroidism was done with regard to symptoms, CAD, other co-morbities like DM, SHT, PVD, CVA, Depression, Dementia, as well as BMI and serum lipid values.

Statistical analysis

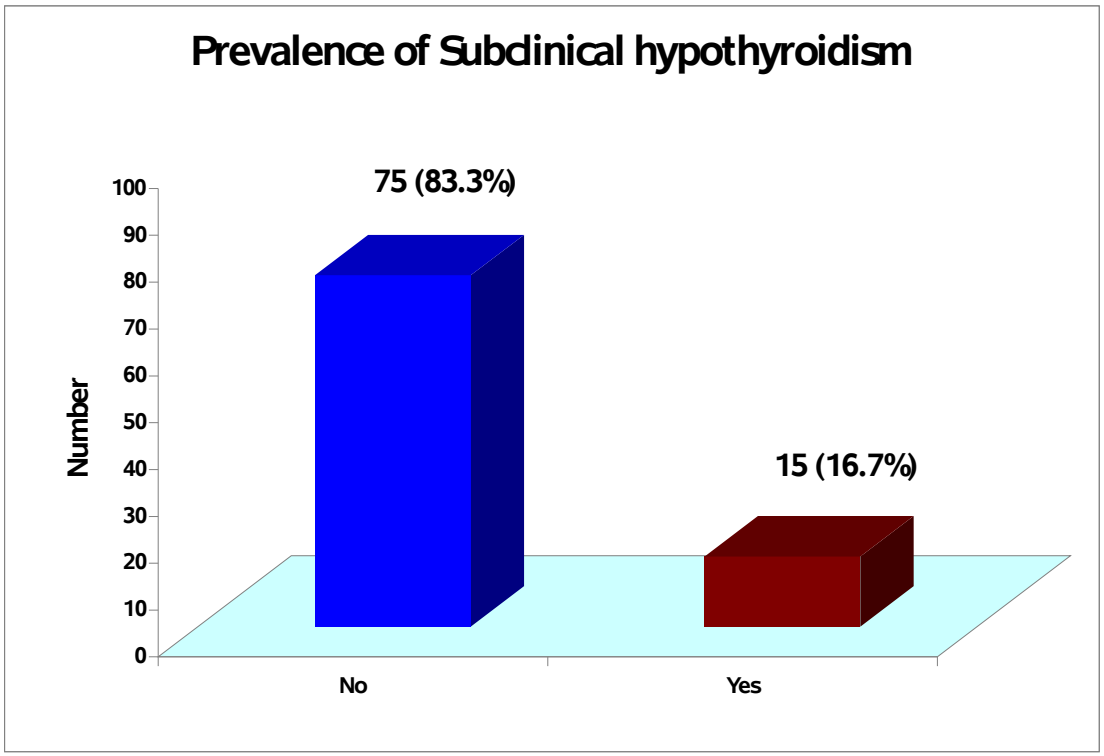
Statistical analysis was done using the Statistical Package for Social Sciences (SPSS). Independent T- test was done in all continuous variables. The chi-square test was used to analyse group difference for categorical variables. A p value of < 0.05 was considered significant.

RESULTS

Prevalence

90 patients were studied and out of these 15 patients (16.7%) were found to have subclinical hypothyroidism.

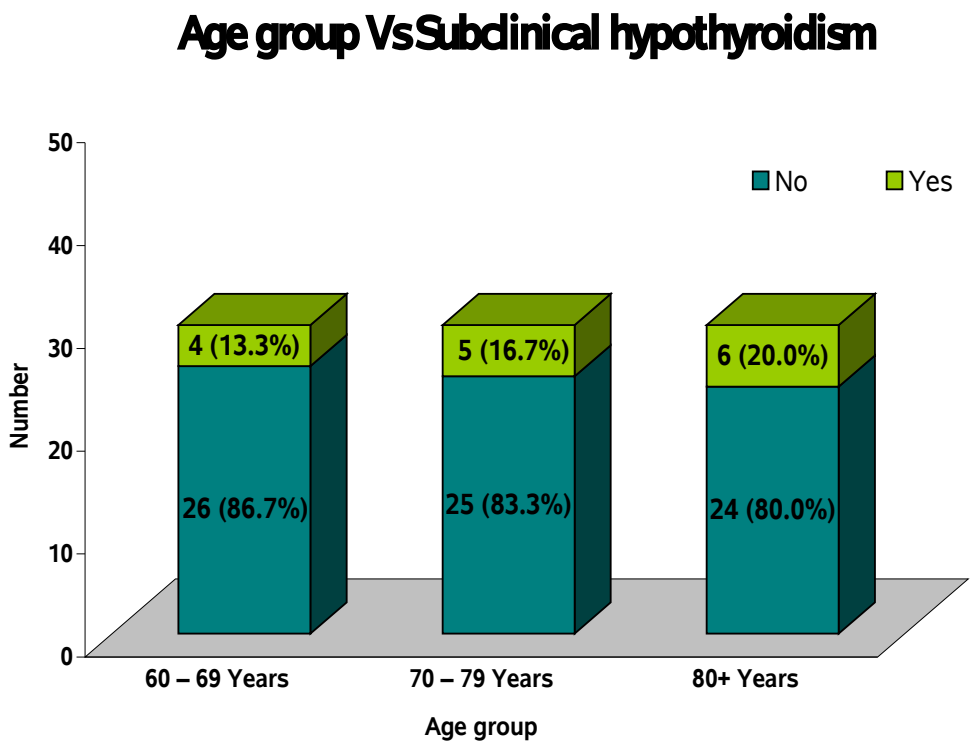
All Age groups	Number (n)	Percentage (%)
No	75	83.3%
Yes	15	16.7%
Total	90	100%



Prevalence in individual age groups

Of the 3 different age groups studied(60-69 yrs, 70-79 yrs, 80+), subclinical hypothyroidism was found in 4,5,6 patients in respective age groups and the others were not found to have subclinical hypothyroidism.

		Subclinical Hypothyroidism		Chi square value	P-value
		No n (%)	Yes n (%)		
Age Group	60 – 69 **Years**	26 (86.7%)	4 (13.3%)	0.480	0.787 (NS)
	70 – 79 **Years**	25 (83.3%)	5 (16.7%)		
	80+ **Years**	24 (80. 0%)	6 (20.0%)		

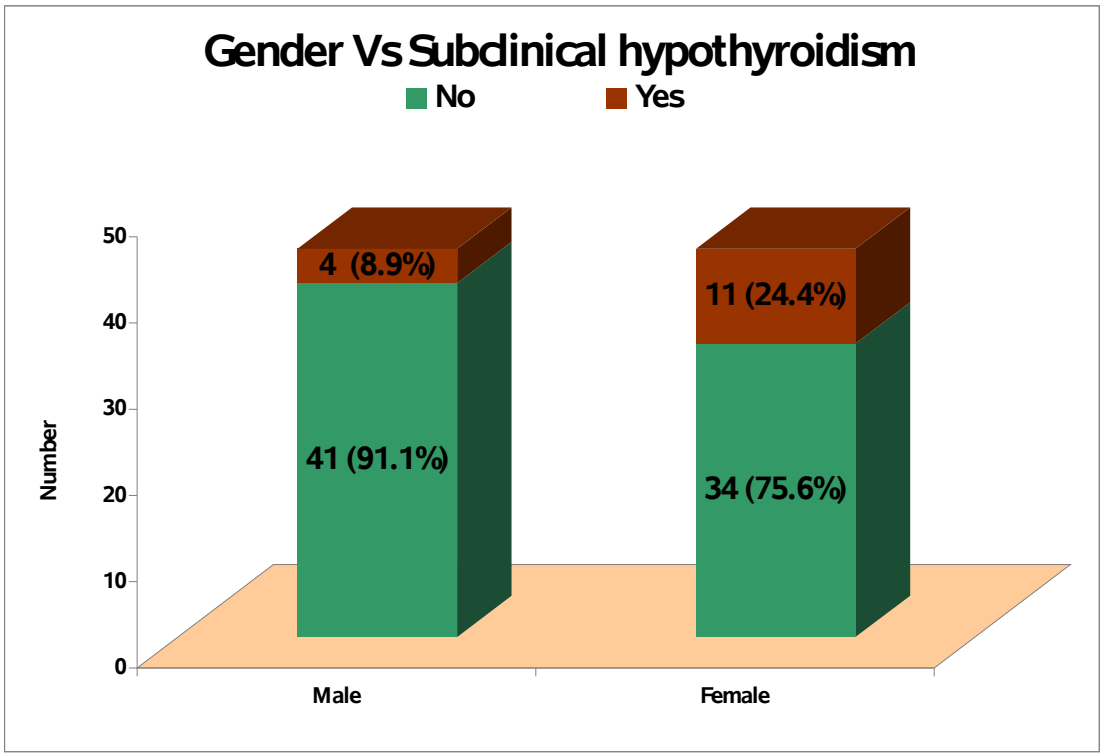


Sex Distribution

11 out of 45females (24.4%) and 4 out of 45 males (8.9%) had subclinical hypothyroidism.

		Subclinical Hypothyroidism		Chi square value	P-value
		No n (%)	Yes n (%)		
Gender	**Male**	41 (91.1%)	4 (8.9%)	3.920	0.048 (Sig)
	Female	34 (75.6%)	11 (24.4%)		

Odds ratio = 3.32; 95% CI (1.00 – 11.36)



Sex and age group distribution

Among the 45 females studied, subclinical hypothyroidism was found in 3,3,5 patients in respective age groups of 60-69 yrs, 70-79 yrs, 80+ yrs and the others were not found to have subclinical hypothyroidism.

		Subclinical Hypothyroidism		Chi square value	P-value
		No n (%)	Yes n (%)		
Age Group	60 – 69 Years	12 (80.0%)	3 (20.0%)	0.963	0.618 (NS)
	70 – 79	12 (80.0%)	3 (20.0%)		

	Years				
	80+ Years	10 (66.7%)	5 (33.3%)		

Of the 45 males studied, 1,1,2 patients in respective age groups of 60-69 yrs, 70-79 yrs, 80+ yrs were found to have subclinical hypothyroidism and not in the others.

		Subclinical Hypothyroidism		Chi square value	P-value
		No n (%)	Yes n (%)		
Age Group	60 – 69 Years	14 (93.3%)	1 (6.7%)	0.549	0.760 (NS)
	70 – 79 Years	13 (86.7%)	2 (13.3%)		
	80+ Years	14 (93.3%)	1 (6.7%)		

Symptom analysis

All subjects:

When the 10 common symptoms of hypothyroidism were studied in all the 90 subjects, no symptoms were acknowledged in 7(7.8%), 1 symptom in 21(23.3%), 2 symptoms in 33(36.7%), 3 symptoms in 18(20.0%), 4 symptoms in 7(7.8%), 6 symptoms in 4(4.4%).

Symptoms Vs Subclinical hypothyroidism

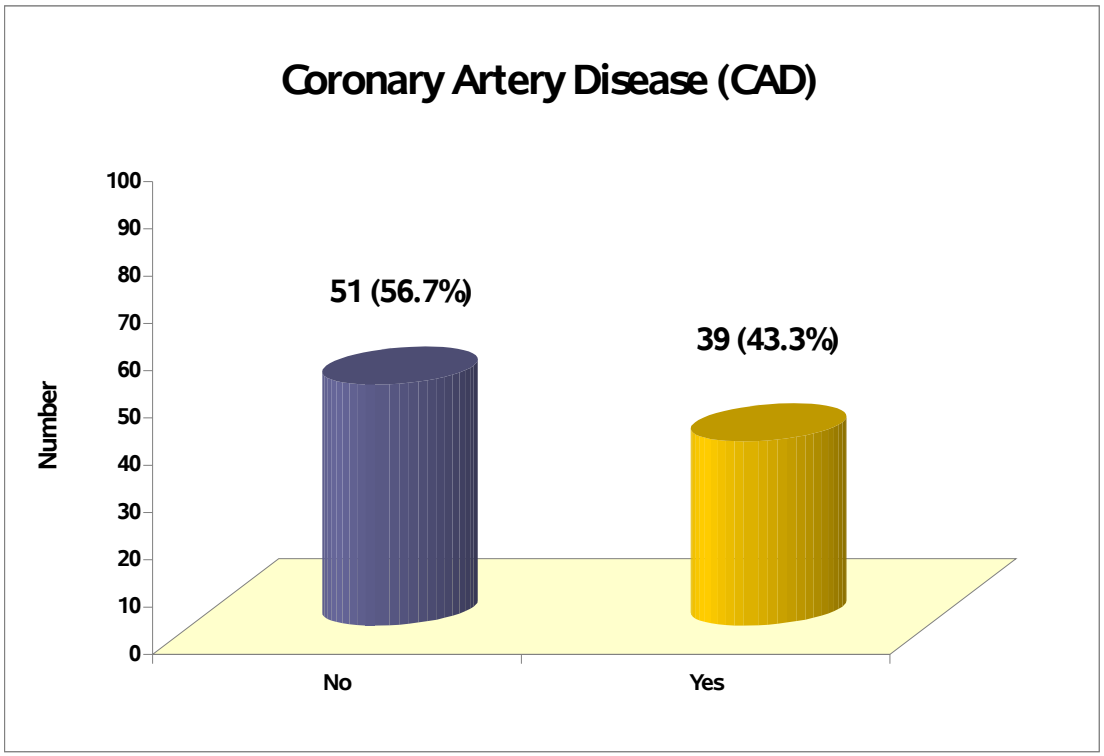
When the same symptoms were studied in subjects with subclinical hypothyroidism, none of them had nil symptom (0%) , 3 had 1 symptom(20.0%), 8 had 2 symptoms(53.3%), 2 had 3 symptoms(13.3%), 1 had 4 symptoms(6.7%) and 1 had 6 symptoms(6.7%).

		Subclinical Hypothyroidism		Chi square value	P-value
		No n (%)	Yes n (%)		
Symptoms out of 10	No symptoms	7 (9.3%)	0 (0%)	3.4 78	0.627 (NS)
	1 symptom	18 (24.0%)	3 (20.0%)		
	2 symptoms	25 (33.3%)	8 (53.3%)		
	3 symptoms	16 (21.3%)	2 (13.3%)		
	4 symptoms	6 (8.0%)	1 (6.7%)		
	6 symptoms	3 (4.0%)	1 (6.7%)		

Coronary Artery Disease

Among the 90 subjects studied, 51(56.7%) did not have Coronary artery disease and 39(43.3%) had Coronary artery disease.

CAD	Number (n)	Percentage (%)
No	51	56.7%
Yes	39	43.3%
Total	90	100%



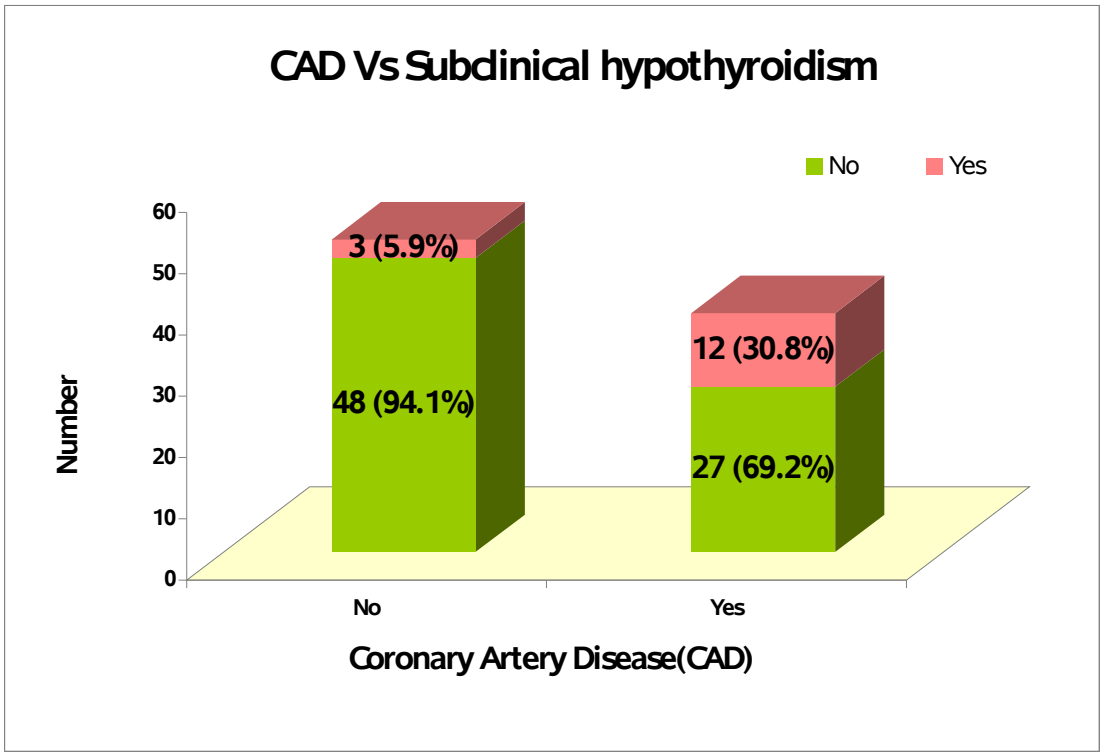
CAD Vs Subclinical hypothyroidism

Among the 39 subjects who had Coronary artery disease, 27(69.2%) did not have subclinical hypothyroidism and 12(30.8%) had subclinical hypothyroidism. Conversely, among the 15 subjects who had subclinical hypothyroidism, 3(20.0%) did not have Coronary artery disease and 12(80.0%) had Coronary artery disease.

		Subclinical Hypothyroidism		Chi square value	P-value
		No n (%)	Yes n (%)		
Coronary Artery	No	48 (94.1%)	3 (5.9%)	9.855	0.002
	Yes	27 (69.2%)	12 (30.8%)		

Disease				(Sig)

Odds ratio = 7.11; 95% CI (1.84 – 27.43)

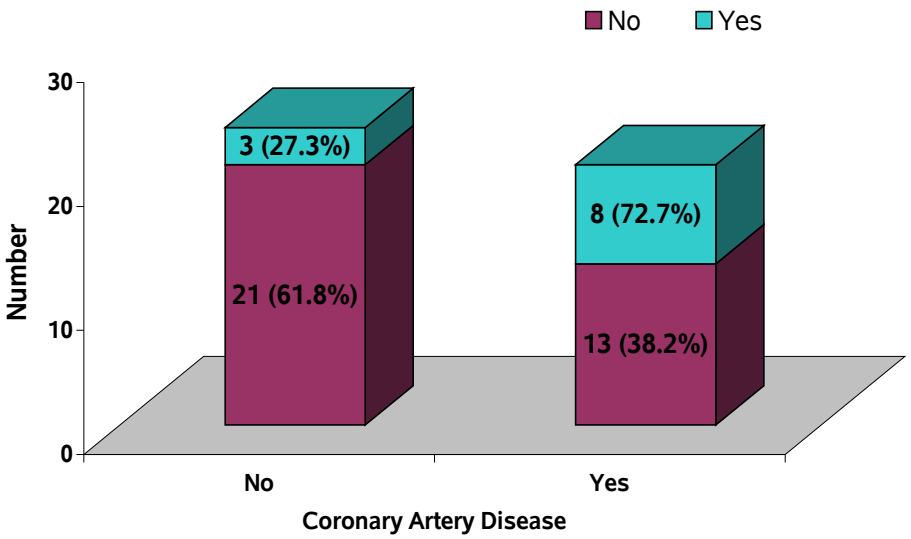


CAD Vs Subclinical hypothyroidism in females

Of the 11 females who had subclinical hypothyroidism, 8(72.7%) had Coronary artery disease and 3(27.3%) did not have Coronary artery disease.

		Subclinical Hypothyroidism		Chi square value	P-value
		No n (%)	Yes n (%)		
Coronary Artery Disease	No	21 (61.8%)	3 (27.3%)	3.973	0.046 (Sig)
	Yes	13 (38.2%)	8 (72.7%)		

CAD Vs Subclinical Hypothyroidism among females



Comorbid illnesses

Among the 90 subjects studied, 29(32.2%) of them had no co-morbidity, 41(45.6%) had single co-morbidity, 18(20.0%) had 2 co-morbities and 2(2.2%) had 3 co-morbidities.

Co-morbidities	Number (n)	Percentage (%)
No co-morbidity	29	32.2%
One co-morbidity	41	45.6%
Two co-morbidities	18	20.0%
Three co-morbidities	2	2.2%
Total	90	100%

Comorbid illnesses Vs Subclinical hypothyroidism

Of the 15 subjects with subclinical hypothyroidism studied, 2 (13.3%) of them had nil, 7 (46.7%) had single co-morbidity, 5 (33.3%) had 2 co-morbities and 5 (33.3%) had 3 co-morbidities.

		Subclinical Hypothyroidism		Chi square value	P-value
		No n (%)	Yes n (%)		
Existing co-morbidities	No co-morbidities	27 (36.0%)	2 (13.3%)		
	1 co-	34 (45.3%)	7 (46.7%)		

	morbidity				
	2 co–morbidities	13 (17.3%)	5 (33.3%)	5.198	0.158 (NS)
	3 co–morbidities	1 (1.3%)	1 (6.7%)		

Analysis of the co-morbidities

Of the co-morbidities, SHT was seen in 44(48.9%) patients and DM in 25(27.8%) patients, CVA & PVD each in 7(7.8%) patients.

Diabetes mellitus Vs Subclinical hypothyroidism

Among the 15 patients with subclinical hypothyroidism, Diabetes mellitus was seen in 6(40.0%) patients.

Systemic Hypertension Vs Subclinical Hypothyroidism

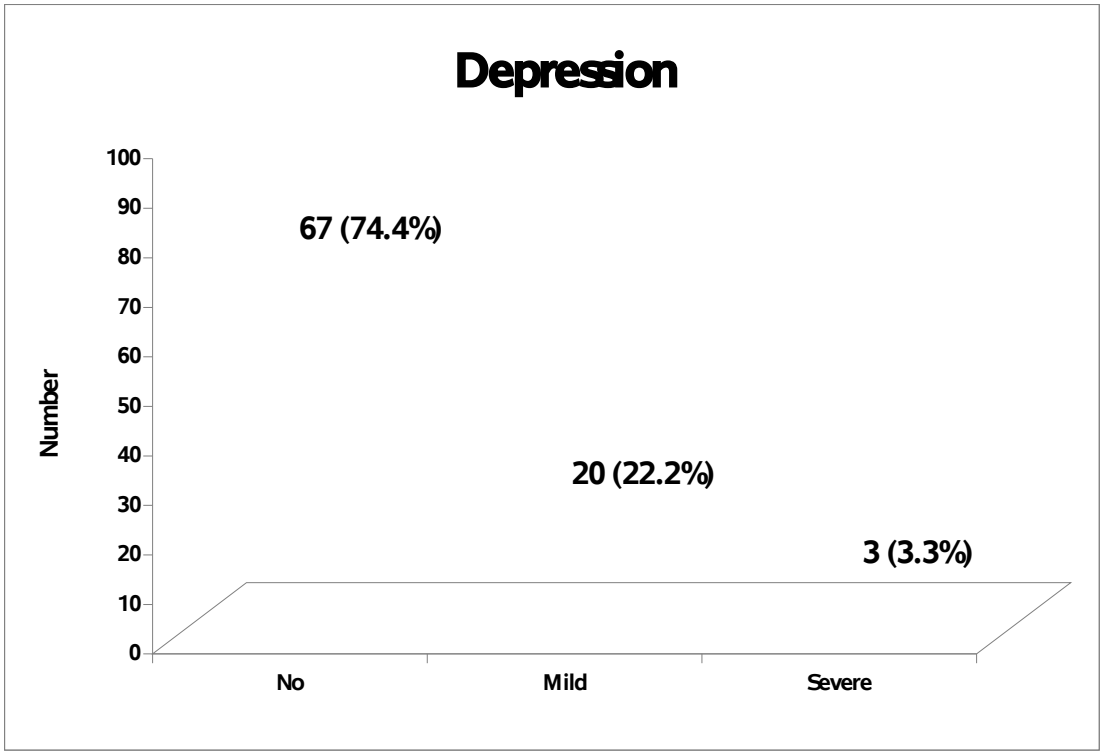
Among the 15 patients with subclinical hypothyroidism, Systemic Hypertension was seen in 10(66.7%) patients.

		Subclinical Hypothyroidism		Chi square value	P-value
		No n (%)	Yes n (%)		
Systemic Hypertension	**No**	41 (54.7%)	5 (33.3%)	2.227	0.131 (NS)
	Yes	34 (45.3%)	10 (66.7%)		

Depression

Among the 90subjects studied, 67(74.4%) were not depressed, 20(22.2%) had mild depression and 3(3.3%) had severe depression.

Age group	Number (n)	Percentage (%)
No	67	74.4%
Mild	20	22.2%
Severe	3	3.3%
Total	90	100%



Depression Vs Subclinical hypothyroidism

Of the 15 subjects with subclinical hypothyroidism, 11(73.3%) had no depression, 4(26.7%) had mild depression and none had severe depression.

	Subclinical Hypothyroidism	Chi square	P-value

		No n (%)	Yes n (%)	value	
Depression	**No**	56 (74.7%)	11 (73.3%)	0.763	0.683 (NS)
	Mild	16 (21.3%)	4 (26.7%)		
	Severe	3 (4.0%)	0 (0%)		

Depression Vs Subclinical hypothyroidism in females

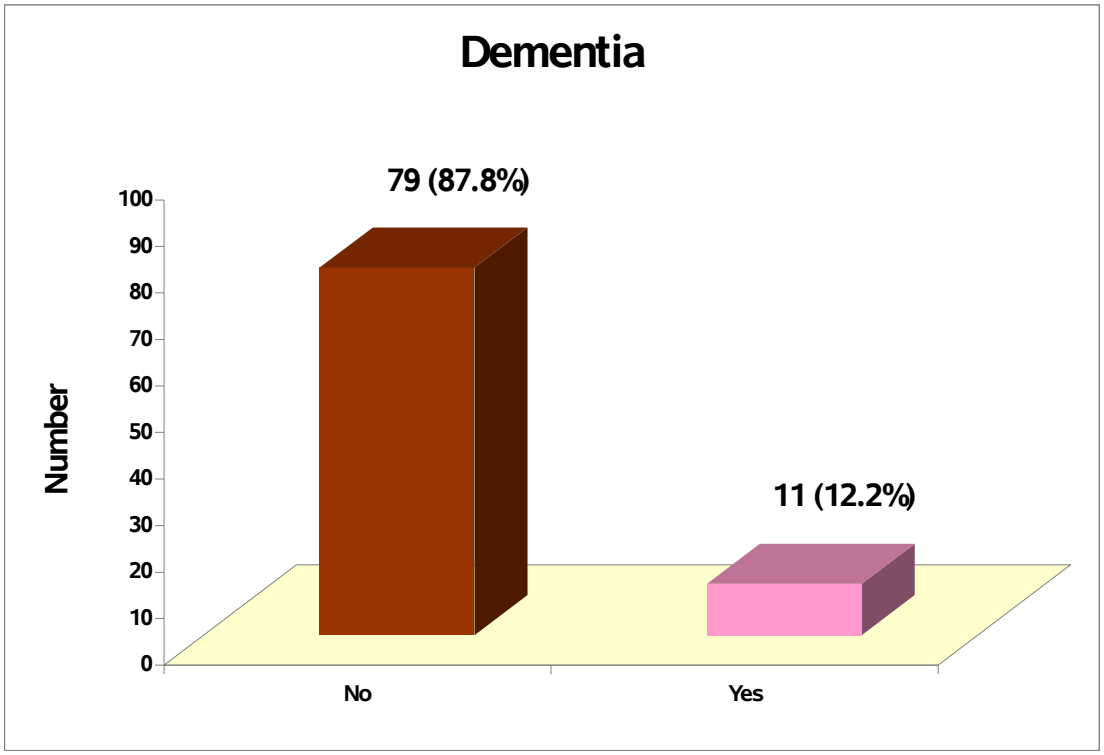
Among the 11 females with subclinical hypothyroidism, 8 (72.7%) had no depression and 3 (27.3%) had mild depression and none had severe depression.

		Subclinical Hypothyroidism		Chi square value	P-value
		No n (%)	Yes n (%)		
Depression	**No**	23 (67.6%)	8 (72.7%)	1.049	0.592 (NS)
	Mild	8 (23.5%)	3 (27.3%)		
	Severe	3 (8.8%)	0 (0%)		

Dementia

Among the 90 subjects studied, 79(87.8%) did not have dementia and 11(12.2%) had dementia.

All Age groups	Number (n)	Percentage (%)
No	79	87.8%
Yes	11	12.2%
Total	90	100%



Dementia Vs Subclinical hypothyroidism

Among the 15 subjects with subclinical hypothyroidism, 13(86.7%) had no dementia, 2 (13.3%) had dementia.

		Subclinical Hypothyroidism		Chi square value	P-value
		No n (%)	Yes n (%)		
Dementia	**No**	66 (88.0%)	13 (86.7%)	0.021	0.886 (NS)
	Yes	9 (12.0%)	2 (13.3%)		

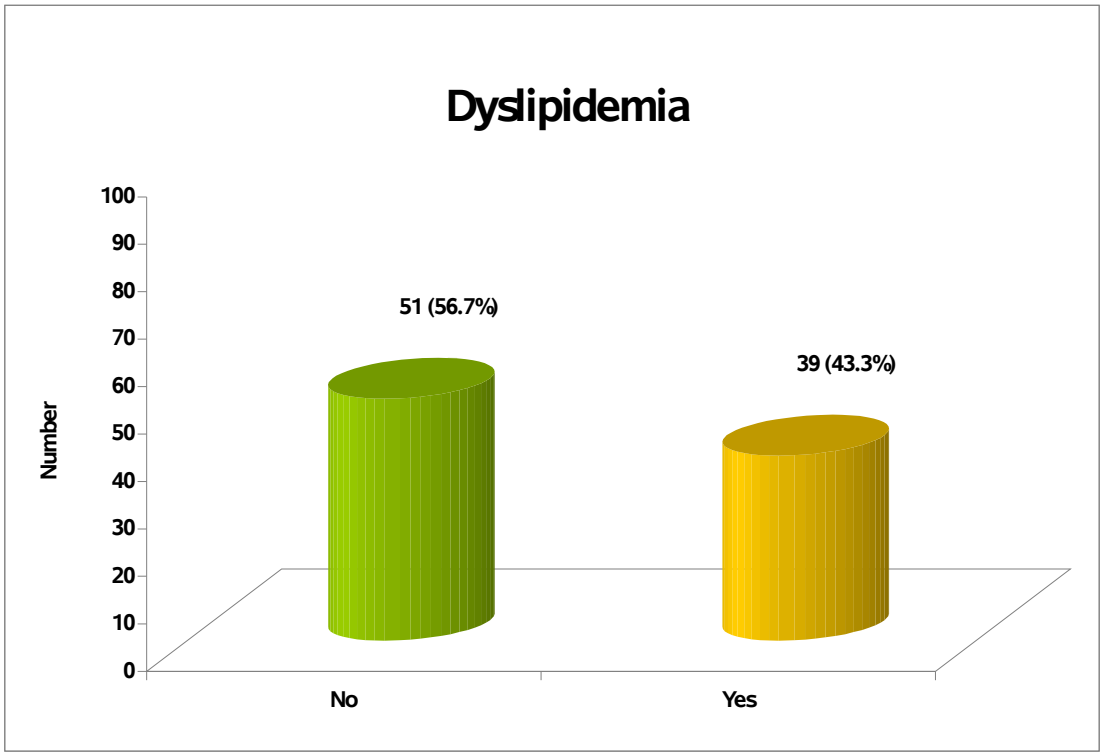
Dementia Vs Subclinical hypothyroidism in females

Among the 11 females with subclinical hypothyroidism, 9(81.8%) had no dementia and 2(18.2%) had dementia.

Dyslipidemia

Among the 90 subjects studied, 51(56.7%) did not have dyslipidemia and 39(43.3%) had dyslipidemia.

All Age groups	Number (n)	Percentage (%)
No	51	56.7%
Yes	39	43.3%
Total	90	100%

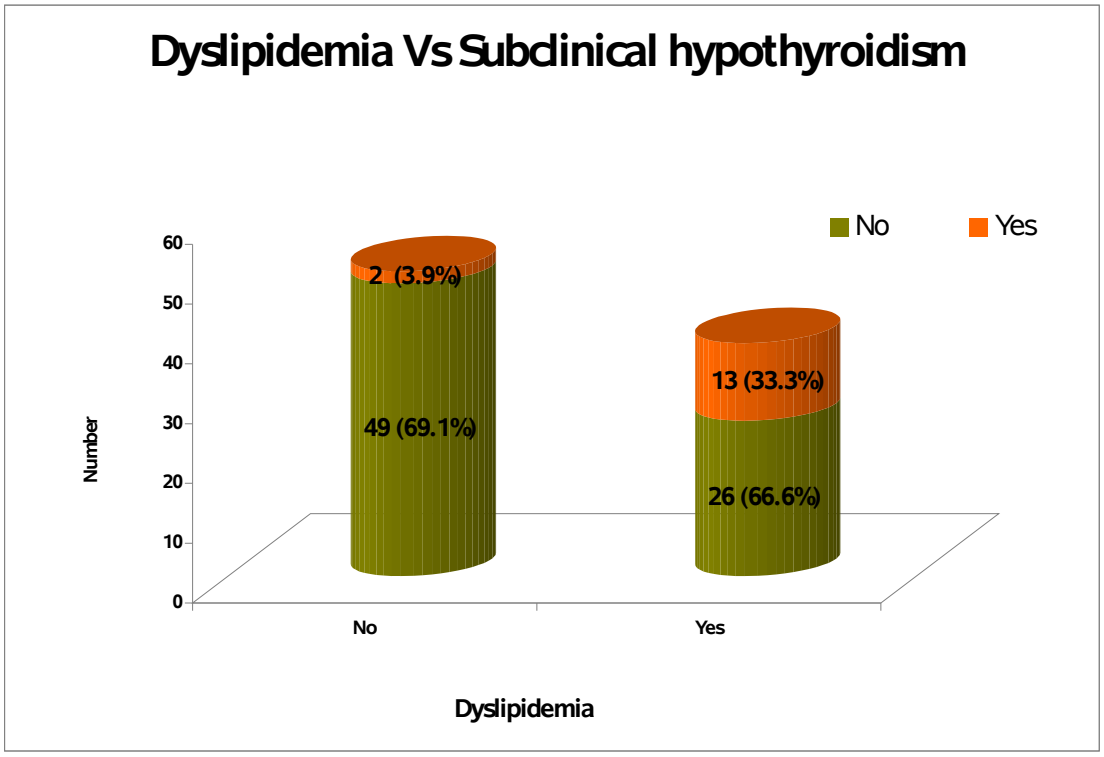


Dyslipidemia Vs Subclinical hypothyroidism

Among the 15 subjects with subclinical hypothyroidism, 13(86.7%) had dyslipidemia, 2(13.3%) had no dyslipidemia.

		Subclinical Hypothyroidism		Chi square value	P-value
		No n (%)	Yes n (%)		
Dyslipidemia	**No**	49 (65.3%)	2 (13.3%)	13.765	<0.001 (Sig)
	Yes	26 (34.7%)	13 (86.7%)		

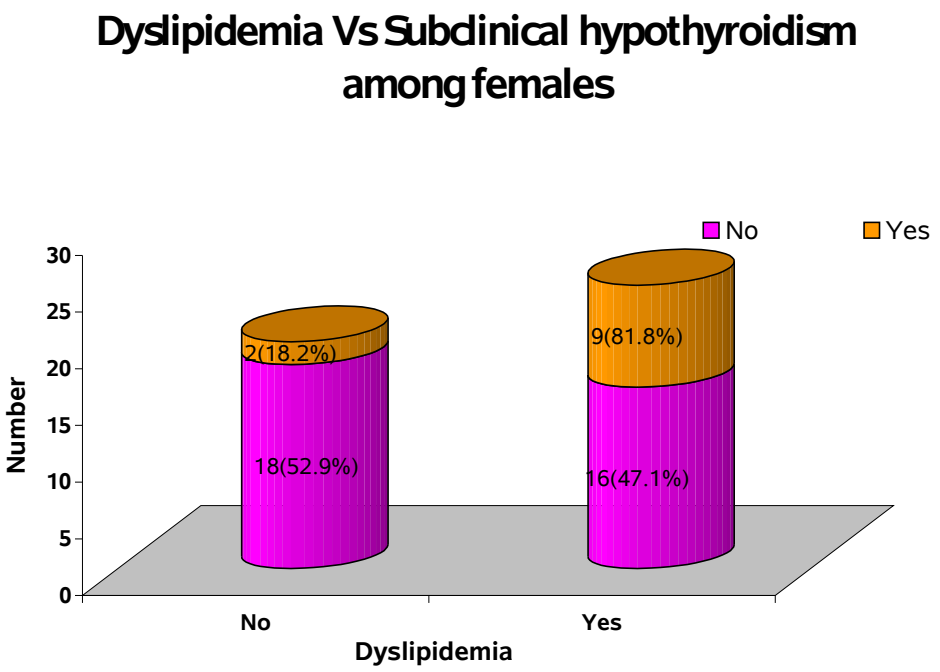
Odds ratio = 12.25; 95% CI (2.57 – 58.46)



Dyslipidemia Vs Subclinical hypothyroidism in females

Among the 11 females with subclinical hypothyroidism, 9(81.8%) had dyslipidemia and 2(18.2%) had no dyslipidemia.

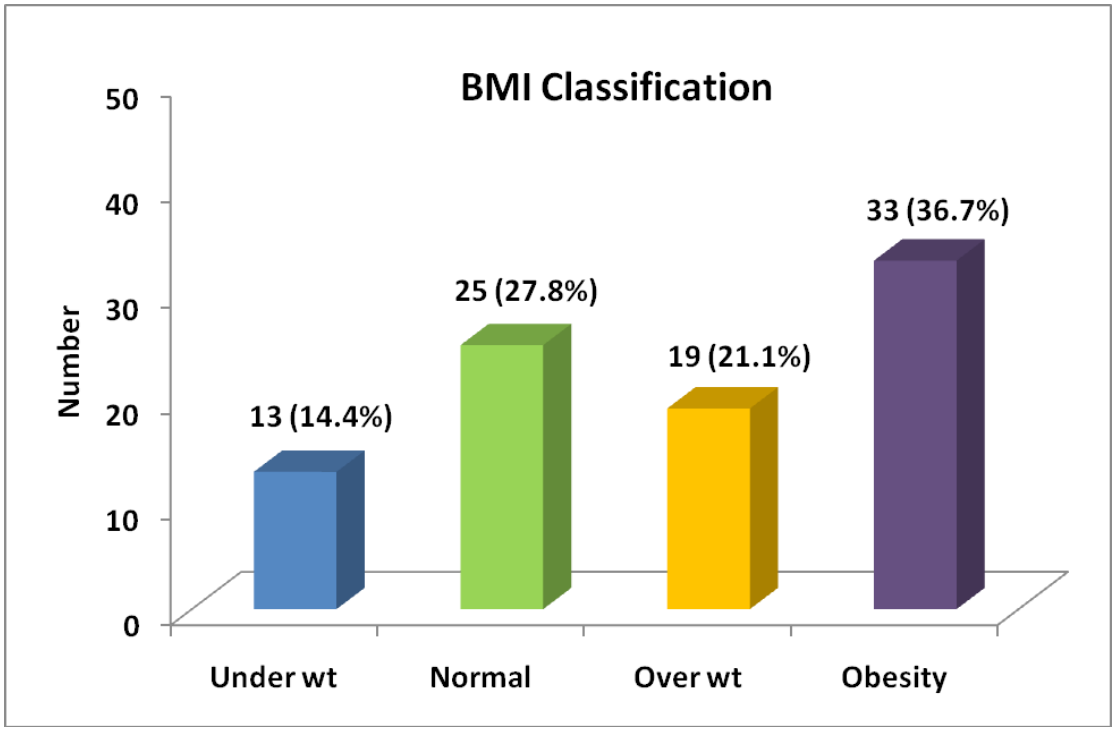
		Subclinical Hypothyroidism		Chi square value	P-value
		No n (%)	Yes n (%)		
Dyslipidemia	**No**	18 (52.9%)	2 (18.2%)	4.067	0.044 (Sig)
	Yes	16 (47.1%)	9 (81.8%)		



BMI (Body Mass Index)

Among the 90subjects studied, 13(14.4%) were under weight, 25(27.8%) were normal, 19(21.1%) were over weight and 33(36.7%) were obese.

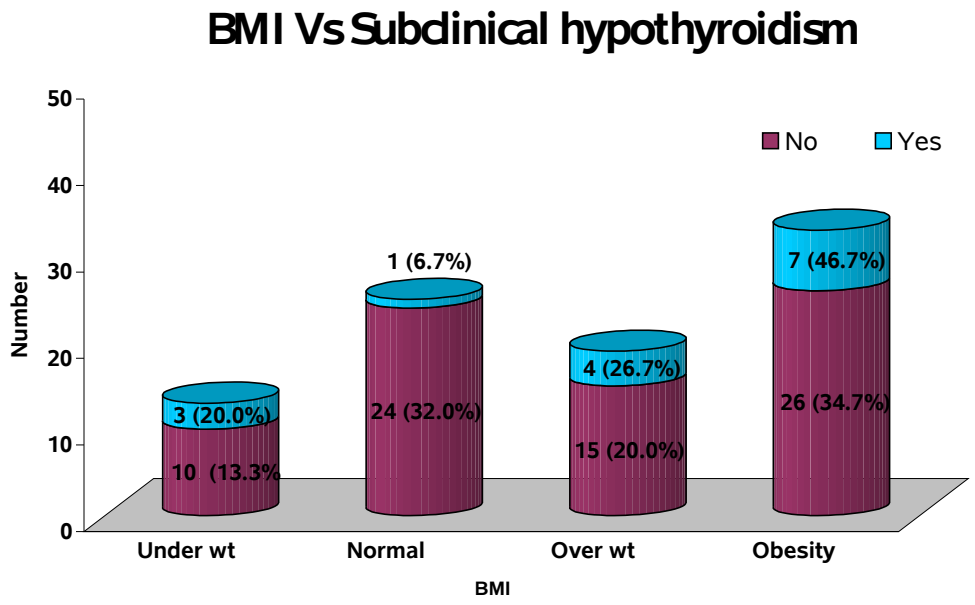
All Age groups	Number (n)	Percentage (%)
Under wt (<18.5)	13	14.4%
Normal (18.5 – 22.99)	25	27.8%
Over wt (23.0 – 24.99)	19	21.1%
Obesity (≥25.0)	33	36.7%
Total	90	100%



BMI Vs Subclinical hypothyroidism

Of the 15 subjects with subclinical hypothyroidism, 3(20.0%) were under weight, 1(6.7%) were normal, 4(26.7%) were over weight and 7(46.7%) were obese.

		Subclinical Hypothyroidism		Chi square value	P-value
		No n (%)	Yes n (%)		
BMI	**Under wt** (<18.5)	10 (13.3%)	3 (20.0%)	4.027	0.259 (NS)
	Normal (18.5 – 22.99)	24 (32.0%)	1 (6.7%)		
	Over wt (23.0 – 24.99)	15 (20.0%)	4 (26.7%)		
	Obesity (≥25.0)	26 (34.7%)	7 (46.7%)		



BMI Vs Subclinical hypothyroidism in females

Among the 11 females with subclinical hypothyroidism, 3(27.3%) were under weight, 0(0%) were normal, 3(27.3%) were over weight and 5(45.5%) were obese.

		Subclinical Hypothyroidism		Chi square value	P-value
		No n (%)	Yes n (%)		
BMI	**Under wt** (<18.5)	2 (5.9%)	3 (27.3%)	6.754	0.080 (NS)
	Normal (18.5 – 22.99)	9 (26.5%)	0 (0%)		
	Over wt (23.0 – 24.99)	6 (17.6%)	3 (27.3%)		
	Obesity (≥25.0)	17 (50.0%)	5 (45.5%)		

BMI Vs Subclinical hypothyroidism in males

Among the 4 males with subclinical hypothyroidism, 0(0%) were under weight, 1(25.0%) were normal, 1(25.0%) were over weight and 2(50.0%) were obese.

		Subclinical Hypothyroidism		Chi square value	P-value
		No n (%)	Yes n (%)		
BMI	**Under wt** (<18.5)	8 (19.5%)	0 (0%)	2.106	0.551 (NS)
	Normal (18.5 – 22.99)	15 (36.6%)	1 (25.0%)		
	Over wt (23.0 – 24.99)	9 (22.0%)	1 (25.0%)		
	Obesity (≥25.0)	9 (22.0%)	2 (50.0%)		

CAD Vs Subclinical hypothyroidism in males

Of the 4 males who had subclinical hypothyroidism, all the 4(100%) had Coronary artery disease.

		Subclinical Hypothyroidism		Chi square value	P-value
		No n (%)	Yes n (%)		
Coronary Artery Disease	**No**	27 (65.9%)	0 (0%)	6.585	0.010 (Sig)
	Yes	14 (34.1%)	4 (100%)		

Dyslipidemia Vs Subclinical hypothyroidism in males

Of the 4 males who had subclinical hypothyroidism, all the 4(100%) had dyslipidemia.

		Subclinical Hypothyroidism		Chi square value	P-value
		No n (%)	Yes n (%)		
Dyslipidemia	**No**	31 (75.6%)	0 (0%)	9.721	0.002 (Sig)
	Yes	10 (24.4%)	4 (100%)		

Depression Vs Subclinical hypothyroidism in males

Among the 4 males with subclinical hypothyroidism, 3(75.0%) had no depression and 1(25.0%) had mild depression and none (0%) had severe depression.

		Subclinical Hypothyroidism		Chi square value	P-value
		No n (%)	Yes n (%)		
Depression	**No**	33 (80.5%)	3 (75.0%)	0.069	0.793 (NS)
	Mild	8 (19.5%)	1 (25.0%)		
	Severe	0	0		

Dementia Vs Subclinical hypothyroidism in males

Among the 4 males with subclinical hypothyroidism, all the 4 (100%) had no dementia.

		Subclinical Hypothyroidism		Chi square value	P-value
		No n (%)	Yes N (%)		
Dementia	**No**	35 (85.6%)	4 (100%)	0.675	0. 411 (NS)
	Yes	6 (14.6%)	0 (0%)		

DISCUSSION

Subclinical hypothyroidism is highly prevalent in elderly and more so in women. The prevalence of 5.9% to 35% has been documented in previous studies, depending on health status, patient characteristics and patient selection procedures. It has been around 5.9% of an unselected population of community-dwelling elderly persons (Sawin et al) and in 9.6% and 14.6% of institutionalized elderly men and women, respectively. The prevalence of subclinical hypothyroidism was found in 6.8% of males and 13.8% of females (Mayer et al 2005).

Subclinical hypothyroidism was found in 11% of 1149 women, mean age 69 years, participating in the Rotterdam Study. Prevalence of hypothyroidism was shown to gradually increase between age 45 and 60 years and to be higher in females, than in males (Canaris et al 2000; Hollowell et al 2002). 35% of the elderly women attended the outpatient clinic had subclinical hypothyroidism in a study conducted in King Abdulaziz University, Saudi Arabia.

In this study of 90 elderly patients in a tertiary care setting, 15 patients (an over all prevalence of 16.7%) were found to have subclinical hypothyroidism. The prevalence increased as the age advances in this study. The prevalence in 60-69 years age group was 13.3%; the prevalence in 70-79 years age group was 16.7%; the prevalence in 80+ years age group was 20.0%. 11 out of 45 females (24.4%) and 4 out

of 45 males (8.9%) had subclinical hypothyroidism. This finding is similar to that of other studies that reported a higher prevalence of subclinical hypothyroidism in elderly women compared with their male counterparts. The prevalence could have been much higher, if the patients with known thyroid dysfunction have also been included.

The rationale for identifying subclinical hypothyroidism in the elderly relates to its potential for progressing to overt hypothyroidism. In a longitudinal study of community-dwelling elders, Rosenthal et al found that 30% of elderly subjects with elevated TSH levels developed overt hypothyroidism over a 4-year period. These studies indicate that TSH measurement in the elderly may provide important information about borderline thyroid function prior to complete thyroid failure.

Some studies have suggested that mild symptoms of hypothyroidism are more prevalent in patients with subclinical hypothyroidism than in age-matched controls. The "classic" clinical signs and symptoms of hypothyroidism are no more frequent in patients with elevated TSH than in the euthyroid elderly. Thyroid status could not be predicted from clinical signs and symptoms in this sample of elderly community-dwelling patients (Bemben et al in 1994).

In this study, 10 common symptoms of hypothyroidism were considered. 29 out of 90 patients had 3 or more number of symptoms, but among them only 4(13.8%) had subclinical hypothyroidism and 8 out of 15 patients with subclinical

hypothyroidism (53.3%) had 2 symptoms. The lack of a relationship between clinical symptoms and thyroid status was further evidenced by the inability of a high frequency of symptoms (≥3) to identify a higher proportion of subclinical hypothyroid patients diagnosed by elevated TSH levels.

The co-morbid illnesses like Diabetes mellitus, Systemic Hypertension, Peripheral vascular disease and Cerebrovascular accidents were also studied in these 90 subjects. Systemic Hypertension was seen in 44 patients (48.9%) and Diabetes mellitus in 25 patients (27.8%), while in the 15 patients with subclinical hypothyroidism, Systemic Hypertension was seen in 10 patients (66.7%) and Diabetes mellitus in 6(40.0%). Co-morbidities typically associated with hypothyroidism were no more significantly prevalent in subclinical hypothyroid patients than in euthyroid patients.

The association of co-morbid illnesses could be further less in the community-dwelling group because the patients attending tertiary care centre would have more ailments than this group. Hypertension is a well known accompanied fact with hypothyroidism and is needed to be studied in a large scale set-up to endorse its relationship with subclinical hypothyroidism.

A 20 year follow-up study of the original Whickham Survey found no association between subclinical hypothyroidism and the development of coronary artery

disease. An association between CAD and subclinical hypothyroidism has been reported in elderly women in the Rotterdam Study. In a study conducted in elderly women and in elderly men in New York Medical College, Valhalla, 11% of CAD patients were associated with subclinical hypothyroidism. Analysis of the relationship between subclinical hypothyroidism and myocardial infarctions in The Rotterdam Study revealed an attributable risk of 60% (subclinical hypothyroidism contributed to 60% of the myocardial infarctions in the women who had subclinical hypothyroidism).

In this study, among the 15 subjects with subclinical hypothyroidism, 3(20.0%) did not have CAD and 12(80.0%) had CAD. Conversely, of the 39 subjects with CAD, 12(30.8%) had subclinical hypothyroidism (p-value 0.002). Of the 11 females with subclinical hypothyroidism, 8(72.7%) had CAD and 3(27.3%) did not have CAD (p-value 0.046). This shows a significant relationship between subclinical hypothyroidism and CAD.

In the above mentioned study conducted in New York Medical College, only two men in the study had subclinical hypothyroidism and both men had electrocardiographic evidence of Q-wave myocardial infarction. In this study, of the 4 males with subclinical hypothyroidism, all the 4(100%) had CAD, showing a very strong relationship between CAD and subclinical hypothyroidism. So, further evaluation is needed and to be performed with large sample size to support the association of subclinical hypothyroidism with CAD in elderly men.

Thyroid Guide Mary Shomon point out that subclinical hypothyroidism is associated with metabolic syndrome. In this study among the 90 subjects, 13(14.4%) were under weight, 25(27.8%) were normal, 19(21.1%) were over weight and 33(36.7%) were obese.

Of the 15 subjects with subclinical hypothyroidism, 3 (20.0%) were under weight, 1(6.7%) were normal, 4(26.7%) were over weight and 7(46.7%) were obese (p-value 0.259). Though there is no significant correlation with increase in BMI and subclinical hypothyroidism, it is prudent to note that only 1 out of 15 (6.7%) subjects with subclinical hypothyroidism had normal BMI and all the others (93.3%) were either under-nourished or over- nourished.

IN A COMMUNITY-BASED CROSS-SECTIONAL SURVEY TO IDENTIFY THE SUBCLINICAL THYROID DYSFUNCTION AND ITS RELATION TO SOCIOECONOMIC DEPRIVATION IN THE ELDERLY BY **SUE WILSON ET AL IN 2006,** AN INDEPENDENT ASSOCIATION BETWEEN THE PREVALENCE OF SUBCLINICAL THYROID DYSFUNCTION AND DEPRIVATION WHICH CANNOT BE EXPLAINED SOLELY BY THE GREATER BURDEN OF CHRONIC DISEASE AND/OR CONSEQUENT DRUG THERAPIES IN THE DEPRIVED POPULATION HAS BEEN IDENTIFIED. IT'S A RENOWN FACT THAT HYPOTHYROIDISM IS ASSOCIATED WITH OBESITY. SO, THE ASSOCIATION OF NUTRITION WITH SUBCLINICAL HYPOTHYROIDISM IS TO BE ESTABLISHED IN NEAR FUTURE.

THE PAQUID SURVEY (1995) AND CORRELATES OF **SUBCLINICAL HYPOTHYROIDISM IN ELDERLY** COMMUNITY RESIDENTS **IN** THE SOUTH WEST OF FRANCE FOUND THAT **IN**CREASED TSH LEVELS WERE SIGNIFICANTLY L**IN**KED WITH FEMALE SEX AND WITH THE PRESENCE OF SYMPTOMS OF DEPRESSION BUT NOT WITH IMPAIRMENT OF COGNITIVE FUNCTION. PSYCHOLOGICAL SYMPTOMS AND QUALITY OF LIVING (QOL) WERE WORSE IN SUBCLINICAL HYPOTHYROIDISM (S.GULSEREN ET AL; 2008).

After the confounding effects of comorbid conditions and use of medications, subclinical thyroid dysfunction was not associated with depression,

anxiety, or cognition (Lesley M. Roberts et al). In this study among the 90 subjects studied, 67(74.4%) were not depressed, 20(22.2%) had mild depression and 3(3.3%) had severe depression. Of the 15 subjects with subclinical hypothyroidism, 11(73.3%) had no depression, 4(26.7%) had mild depression and none had severe depression (p-value 0.683) failing to endorse the relationship of depression with subclinical hypothyroidism.

Among the 90 subjects studied, 79(87.8%) did not have dementia and 11(12.2%) had dementia. Among the 15 subjects with subclinical hypothyroidism, 13(86.7%) had no dementia, 2 (13.3%) had dementia (p-value 0.886). Thus, the association between dementia and subclinical hypothyroidism could not be established.

The Colorado Thyroid Disease Prevalence Study shown the mean serum total cholesterol levels in the 22,842 euthyroid subjects (216 mg/dl), the 2,336 subclinical hypothyroidism subjects (224 mg/dl), and the 114 subjects with overt hypothyroidism (251 mg/dl); both thyroid disease groups had statistically higher total cholesterol levels (data not shown) than did the euthyroid controls ($P < 0.001$).

In a study done to evaluate the serum lipid level alterations in subclinical hypothyroid patients in Gorgan by Azad Reza Mansourian et al, the serum total cholesterol concentrations were higher in subjects with subclinical hypothyroidism than in euthyroid subjects significantly.

In this study, among the 90 subjects studied, 51(56.7%) did not have dyslipidemia and 39(43.3%) had dyslipidemia and of the 15 subjects with subclinical hypothyroidism, 13(86.7%) had dyslipidemia, 2 (13.3%) had no

dyslipidemia (p-value<0.001). Among the 11 females with subclinical hypothyroidism, 9 (81.8%) had dyslipidemia and 2 (18.2%) had no dyslipidemia (p-value 0.044). Of the 4 males who had subclinical hypothyroidism, all the 4 had dyslipidemia (p-value 0.002). This shows a significant relationship between dyslipidemia and subclinical hypothyroidism both in elderly males and females.

IN THIS STUDY, A**LL THE MEN WITH SUBCLINICAL HYPOTHYROIDISM WERE FOUND TO HAVE BOTH CAD AND DYSLIPIDEMIA.** IN A STUDY OF RISK FOR ISCHEMIC HEART DISEASE AND ALL-CAUSE MORTALITY IN SUBCLINICAL HYPOTHYROIDISM IN JAPAN BETWEEN 1984 AND 1987 AND FOLLOWED BY A 10 YEAR FOLLOW-UP STUDY UNTIL 1998, INCREASED MORTALITIES FROM ALL CAUSES AFTER BASELINE MEASUREMENT WERE APPARENT IN MEN WITH SUBCLINICAL HYPOTHYROIDISM (HAZARD RATIO, 1.9 TO 2.1) BUT NOT IN WOMEN, ALTHOUGH SPECIFIC CAUSES OF DEATH WERE NOT DETERMINED **(MISA IMAIZUMI ET AL).**

IN THIS JUNCTURE, IT IS TO BE EMPHASISED THAT LARGE-SCALE RANDOMISED, PROSPECTIVE CONTROLLED STUDIES WITH FOLLOW UP NEEDED TO BE DONE IN ELDERLY MEN WITH SUBCLINICAL HYPOTHYROIDISM TO IDENTIFY THE CAUSAL ROLE OF SUBCLINICAL HYPOTHYROIDISM IN CORONARY ARTERY DISEASE AND DYSLIPIDEMIA.

CONCLUSION

- The prevalence of subclinical hypothyroidism is considerably high in this study (16.7%). The prevalence increases as the age advances. The prevalence is more in females than in males.
- Coronary artery disease and dyslipidemia are significantly associated with subclinical hypothyroidism.
- Body Mass Index shares a place in evaluation of subclinical hypothyroidism.
- There is a lack of relationship between clinical symptoms and the thyroid status in elderly.
- The study failed to endorse the association of subclinical hypothyroidism with co-morbid illnesses, depression and dementia.
- The cross-sectional nature of this analysis makes it difficult to ascribe causality to any associations found. Because we do not know whether thyroid test abnormalities preceded elevations in lipid levels and coronary artery disease, it cannot be definitely stated that one leads to the other. Further evaluation of this relationship with longitudinal data would be necessary to support a causal link.
- The evaluation of patients from population-based screening programs who are found to have subclinical hypothyroidism rather than those referred for specialty management would be useful in determining the magnitude of the disease.

- The thyroid disease should be considered during routine evaluation of this susceptible group and should be followed by appropriate detection and treatment.
- Further research may determine whether treatment of subclinical hypothyroidism will benefit in preventing adverse health outcomes.

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PROFORMA

NAME: **ADDRESS:**

AGE/SEX:

IP/OP/GM NO:

PREVIOUS OCCUPATION:

INCOME: **PHONE/MOBILE NO:**

SYMPTOMS:

Fatigue	Y/N	Dry skin	Y/N
Weakness	Y/N	Hair loss	Y/N
Weight gain	Y/N	Constipation	Y/N
Edema	Y/N	Cold intolerance	Y/N
Excessive sleep	Y/N	Paraesthesia	Y/N

H/O intake of Antithyroid drugs Y/N **H/O intake of Thyroxine Y/N**

Coronary artery disease : Y/N

If yes, then no. of years :

Other comorbid illness:

PVD : Y/N **DM : Y/N**

CVA : Y/N **SHT : Y/N**

Height : cm **Weight : kg**

Pulse : /min **BP : mm/Hg**

ECG : **Ankle jerk :**

GERIATRIC DEPRESSION SCALE

- Are you basically satisfied with your life? Y/**N**
- Have you dropped many of your activities and interests? **Y**/N
- Do you feel that your life is empty? **Y**/N
- Do you often get bored? **Y**/N
- Are you in good spirits most of the time? Y/**N**
- Are you afraid that something bad is going to happen to you? **Y**/N
- Do you feel happy most of the time? Y/**N**
- Do you often feel helpless? **Y**/N
- Do you prefer to stay home, rather than going out and doing new things? **Y**/N
- Do you feel you have more problems with memory than most? **Y**/N
- Do you think it is wonderful to be alive now? Y/**N**
- Do you feel pretty worthless the way you are now? **Y**/N
- Do you feel full of energy? Y/**N**
- Do you feel that your situation is hopeless? **Y**/N
- Do you think that most people are better off than you are? **Y**/N

CDT & MINI-COG

Positive **0/1 or 2 with aCDT**

Negative **3/1 or 2 with nCDT**

LIPID PROFILE:

Total cholesterol : mg/dl LDL : mg/dl

Triglycerides : mg/dl HDL : mg/dl

THYROID PROFILE:

TSH : µIU/ml FT4 : ng/dl

ABBREVIATIONS

TSH	Thyroid stimulating hormone
FT4	Free Thyroxine
FT3	Free Triiodothyronine
TRH	Thyrotropin Releasing Hormone
TBG	Thyroxine-binding globulin
TTR	Transthyretin
TR	Thyroid hormone receptors
rT3	reverse T3
NTI	Non- thyroid illness
Lp a	Lipoprotein a
TC	Total cholesterol
HDL	High Density Lipoprotein
LDL	Low-density lipoprotein
TG	Triglycerides
CAD	Coronary Artery Disease
DM	Diabetes Mellitus
SHT	Systemic Hypertension
PVD	Peripheral Vascular Disease
CVA	Cerebrovascular Accident
CDT	Clock drawing test
BMI	Body Mass Index
SYMP	Number of Symptoms
NS	Not Significant
Sig	Significant
yrs	years
GDS	Geriatric Depression Scale